HYPERPYREXIA

IN

RHEUMATISM

BY

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HYPERPYREXIA IN RHEUMATISM

I HAVE intentionally chosen the above title rather than "Hyperpyrexia in Rheumatic Fever," since my object will be to consider the condition which is thus commonly designated from a somewhat wider aspect than is implied by the use of the latter phrase.

Rheumatic fever has for so long been regarded as the chief type of the disease we call rheumatism, and the clinical condition which we are about to consider has been so recognised as occurring uniformly in this typical form of rheumatism, that, not unnaturally, writers upon the subject have practically confined their attention to an investigation of *Hyperpyrexia in Rheumatic Fever*. Thus the elaborate report of the Clinical Society of London has for its title: "Report of a Committee of the Society nominated to investigate the Causes, Consequences, and Treatment of Hyperpyrexia in Rheumatic Fever and other acute Febrile Diseases" (7). But in recent years, more especially as a consequence of the investigations and writings of Cheadle and others, a greater attention has been paid to the manifestations of rheumatism other than that type known as rheumatic fever; and the view put forward by Cheadle (4) that the true picture of the disease is to be found in rheumatism as it manifests itself in *children* rather than the rheumatic fever of *adult* life has been recently supported by others. Thus Stephen Mackenzie says (19)[1]: "If we wish to arrive at a proper conception of what should be regarded as rheumatism, we must study its phenomena at various ages, and pay particular attention to the disease as it occurs in childhood and early life." Certainly by adopting the point of view advocated by those writers, the question of the occurrence of hyperpyrexia in the disease acquires fresh interest, and it is largely because previous investigators of the condition have restricted their attention almost entirely to the consideration of its bearings upon the characteristic phenomena of the rheumatic fever of *adults*, that I have been led, not only to choose the somewhat wider subject of "Hyperpyrexia in Rheumatism" for my title, but also to examine the condition in the light of this interpretation.

[1] p. 32.

It has been known for more than a century that a patient suffering from an attack of acute or even subacute rheumatism, which may have been apparently following the usual course of the disease under the method of treatment which might be in vogue at the period, was occasionally seized with a condition characterised by restlessness, delirium, sometimes convulsions, and ending usually in coma, these cerebral symptoms being accompanied by feeble and rapid cardiac action, with stertorous respiration, which speedily ended in death. Prior to the days of clinical thermometry, such cases were generally looked upon as instances of metastasis of the rheumatism to the meninges of the central nervous system, and to them the term "cerebral rheumatism" was applied. When, however, it was announced by Kreuser in 1866 and Ringer in 1867 that these cases were frequently characterised by a very high temperature, the term "Rheumatic Hyperpyrexia" was given to them, the symptoms of cerebral and general systemic disturbance being ascribed to the high temperature. Consideration of the various theories as to the significance and causation of the condition will be more conveniently postponed to a subsequent portion of this paper, but enough has been said to show that at the very outset a difficulty presents itself, viz., with what meaning is the phrase "Hyperpyrexia in Rheumatism" to be used.

The difficulty arises from the fact that in various contributions to an investigation of the subject, the term Rheumatic Hyperpyrexia is applied to different conditions. According to its *literal* meaning, the essential at all events should be *excessive* pyrexia. But in the Clinical Society's Report (7)[1] for the investigation of "Hyperpyrexia in Rheumatic Fever" a description and analysis is given of a group of cases "*without marked excess of temperature*," though "showing the symptoms well-marked which usually characterise the hyperpyrexial cases"; while another and larger group of cases is also considered which showed "a marked tendency to high range of temperature, viz., 104°, continued and persistent." On the other hand, in the "Report of the Collective Investigation Committee of the British Medical Association on Acute Rheumatism" (8)[2] we find only cases are included under the heading of hyperpyrexia "in which the temperature at any time exceeded 107°." Thus in the latter case the actual range of the temperature is the standard by which the cases are judged, while in the former the whole clinical phenomena are taken into account, with the result that so-called "hyperpyrexial" cases *may never have shown any hyperpyrexia*. In fact the term is used as practically synonymous with the old phrase "Cerebral Rheumatism."

[1] p. 262. [2] p. 401.

But even if the phrase be restricted entirely to cases of *literal* "*hyper-*" (excessive) pyrexia, there is still the further difficulty of deciding at what limit pyrexia becomes "excessive." Wunderlich, in his classical work (27),[1] speaks of temperatures as hyperpyretic "which in every known disease, except relapsing fever, in all probability indicate a fatal termination," giving as his limit 42° Centigrade [107·6° Fahr.] or more. Fagge, in speaking of pyrexia and its classification, follows Wunderlich so far, but gives no decided opinion on the point at which the term hyperpyrexia should be employed, his statement (13)[2] being indeed very vague: "it is generally understood to mean such a temperature as is sufficient of itself to endanger life if continued for any length of time." Sturges, on the other hand, in his paper on the "Temperature of Young Children in Health and Disease" (26), adopts 105·5° as his pyrexial limit, and thus the point of commencement of hyperpyrexia. It seems therefore impossible to discover any point agreed upon by all at which pyrexia passes into hyperpyrexia, but perhaps it will suffice for practical purposes if in this paper *105·5°* be regarded as fixed upon arbitrarily as the limit beyond which the temperature is regarded as hyperpyrexial, the essentially important points being the tendency of the temperature to rise still higher, and the fact that the patient's life is in immediate danger.

When, in a subsequent portion of this paper, the consideration of the etiology of hyperpyrexia is reached, we may be able to arrive at a more accurate *definition* of the term, but with the above as a working postulate I shall now proceed to give a summary of the notes of the first case of the condition which came under my notice while acting as house-physician at Leith Hospital. (Another case which occurred three weeks later—also in Leith Hospital—in which the patient recovered under prompt treatment with ice packs, will be recorded when describing the influence of the number of rheumatic attacks upon the recurrence of hyperpyrexia; while a brief note of other two cases, which have also occurred in Leith Hospital, will be given when dealing with the character of the rheumatic attack and the mode of onset respectively.)

Case I.—A. P., aged thirty-one, a grainweigher, had been suffering for fully ten days from the symptoms of an ordinary attack of rheumatic fever. Dr Garland—to whom I am indebted for many of the details of the case—states that this was at least his second if not his third attack of the same complaint, and under treatment with the salicine compounds he was progressing favourably. On October 19th, 1889, however, when his medical attendant visited him as usual in the forenoon, the patient stated

[1] p. 7. [2] Vol. i. p. 31.

that he felt quite well, his pains being entirely gone. His temperature (in the mouth) was found, however, to be 107°. Dr Garland at once informed him of the dangerous condition in which he was, and advised his immediate removal to Leith Hospital, a proposal to which the patient was strongly averse, because he insisted that he was cured, and it was not till after considerable discussion that he consented. On admission to the Hospital half an hour later, viz., at 10.50 A.M., he was in a state of absolute unconsciousness with stertorous breathing, very rapid, thready pulse, and immobile, somewhat contracted pupils. Very marked miliary rash with sudamina present over the whole body. At 11 A.M. he was placed in a bath with water at the temperature of 90° F. cooled down rapidly to 75° by means of ice, and notwithstanding this his temperature (as taken in the rectum by three different thermometers) remained at 110° for twenty-five minutes before it fell even to 109·4°. [It was unfortunate that none of the thermometers at hand at the time were constructed to register higher than 110°. for, looking to the fact that fully twenty minutes elapsed before the temperature fell below this point, it was doubtless really higher than this. Although each of the thermometers used was an ordinary "five minute" one, the maximum register of the instrument was in each case attained within half a minute of its insertion into the rectum.] At 11.30 A.M., the rectal temperature having fallen to 108·2°, patient was removed from the bath and placed on a bed with merely a sheet over him, which was then covered with ice. His temperature now fell steadily, about 1° every five minutes, and at noon he was removed to a dry bed, his oral temperature being then 101° and 99° a few minutes later. His pulse was now much stronger, respiration, however, still stertorous, and the patient practically quite unconscious. From this time onwards until his death, seven days later, his progress briefly stated was as follows :—

1. *General condition.*—Within an hour after his removal from the bath, a peculiar trembling began in the arms, and, gradually involving the whole body, was at times so violent as almost to resemble the clonic stage of epilepsy, there being, however, no foaming at the mouth, biting of the tongue, or other sign of epilepsy. This passed off slowly in about three hours. On the morning of the 20*th* (*i.e.* next day), patient for the first time spoke quite intelligently, saying in reply to questions that he had "no pain anywhere," "felt comfortable," etc., and he said "good morning" to the nurse quite distinctly. His urine was found to be albuminous, but no casts were detected. At night pericardial friction was observed for the first time.

21*st Oct.*—Friction to-day well marked over the base of the

heart. Patient spoke to his wife apparently quite intelligently, but said he did not know her. Casts found in the urine to-day. From this time onwards he was never again sensible, talking frequently, but always in a "wandering," delirious manner.

23*rd Oct.*—Blood as well as casts present in the urine to-day. Patient, who was often very restless and occasionally rather violently delirious, got very gradually weaker, and died quietly on the 26th October, the *eighth* day after admission.

2. *Temperature.*—Broadly speaking, an ice-cap to the head sufficed at first to keep the temperature from rising. Then an abdominal ice-pack was resorted to with success, various drugs being of no avail, viz., antipyrin, antifebrin and sodium salicylate. Latterly the abdominal ice-pack failed to act at once,—an hour often elapsing ere any fall in the temperature was noted,—the general ice-pack, however, always proving of immediate benefit.

Such being the condensed and rather imperfect record of the case which forms, as it were, my text, I shall next proceed to consider the subject of rheumatic hyperpyrexia in reference to several points.

1. *Frequency.*—On this point it is very difficult to get accurate information, but that it is not altogether rare is evident from the fact mentioned by Fagge (13)[1] that in Guy's Hospital alone at least fourteen deaths occurred from this cause in seven years. Hospital records, no doubt, frequently indicate what number of their cases of rheumatism developed hyperpyrexia. It must, however, always be borne in mind that patients may be sent to hospital (as in three of the five instances I shall record) *because of* hyperpyrexia either actually present or suspected to be impending, and hence the proportion of hyperpyrexial cases may appear unduly high in statistics based merely on hospital cases.

One would require figures based on cases treated at home in private practice; and while this is what we get in the Collective Investigation Record of the British Medical Association, the total number of cases, 655 in all, is much too small to draw deductions from for the purpose of averages. Amongst these 655 cases of rheumatism, four are described as hyperpyrexial, a percentage of ·61. But, as before mentioned, a temperature of 107° is taken in this report as the limit required to be passed to admit the cases within this group. Now in the list of *fatal* cases in the same report, two are described as having had temperatures of 105·6° and 105·8° respectively, so that the percentage is raised to ·91 if these also are admitted as being within the hyperpyrexial category according to the arbitrary limit agreed on in this paper; while there might possibly be still others with temperatures above 105·5° which are not specially mentioned in the report because they were not fatal.

[1] Vol. ii. p. 697.

On the other hand, it is quite possible that the frequency is in reality much *less* than would appear from the Collective Investigation Record; for, apart from the probability that medical men having such cases would be much more likely to forward them to the Committee than others who had merely numerous mild or ordinary cases, it is very noteworthy that out of the 655 cases there are reported only thirty-two cases of rheumatism under the age of ten (the figures for quinquennial periods are not given). Since hyperpyrexia, as we shall see, is practically unknown in children, it is evident that had the statistics comprised more children, in conformity with the acknowledged frequency of the disease amongst them, the percentage frequency of hyperpyrexia in rheumatism would then almost certainly be much less.

The same difficulty meets us in dealing with statistics of cases treated in hospitals, for while the returns of rheumatism in *children's* hospitals show practically no cases of hyperpyrexia, *adult* hospital reports, again, give statistics of percentages which are vitiated by the facts above referred to. Hence it is evident that hospital statistics in regard to hyperpyrexia are apt to be invalidated to a considerable extent by the fact (1) that cases of rheumatism are sent to hospital because of hyperpyrexia, (2) they usually give averages based upon only adult cases of rheumatism. To illustrate how hospital statistics vary, I may refer to the elaborate paper of Dr J. H. Bryant on "One Hundred Cases of Hyperpyrexia" (3), in which only cases of temperature above 106° are taken. In this he states[1] that "between the years 1879 and 1893, inclusive, 1821 patients suffering from acute rheumatism were admitted to Guy's Hospital; and of these seven, or ·38%, suffered from hyperpyrexia." Compare with this the fact mentioned in the Clinical Society's Report (7),[2] that out of the 1300 cases of rheumatism treated in Middlesex Hospital during the years 1870-79 inclusive, no less than 22 were cases of hyperpyrexia, a percentage of almost 1·7%.

There seems little doubt that rheumatic hyperpyrexia shows the effect of what might be termed a "*seasonal*" influence as regards its period of occurrence. In so far as regards its frequency in the various months of the year statistics have almost uniformly shown that it is most prone to occur, in this country at least, in the warmer months of the year—June to September. Thus to take only the most recent collection of cases (3),[3] in Bryant's analysis of 83 cases of rheumatic hyperpyrexia, collated from various sources, 50·7% of those in which the date was given were found to have occurred during these four months, thus leaving 49·3% for the other eight months. This is all the more striking in view of the fact that the *prevalence of rheumatism*

[1] p. 389. [2] p. 263. [3] p. 399.

is at its *lowest* at this season of the year, as is shown in the following table (taken from the Clinical Society's Report (7),[1] the percentages for the prevalence of rheumatism being calculated upon 1300 consecutive cases of that disease in Middlesex Hospital.

	Cases of Hyperpyrexia.	Cases of Rheumatism.
Spring (March, April, May) .	11 or 17%	306 or 23%
Summer (June, July, August) .	25 „ 39%	296 „ 22%
Autumn (Sept., Oct., Nov.) .	18 „ 28%	371 „ 28%
Winter (Dec., Jan., Feby.) .	10 „ 16%	362 „ 27%

Thus cases of hyperpyrexia are most frequent when the cases of rheumatism are at their minimum.

Some evidence has also been adduced to show that cases of hyperpyrexia occur more frequently *in certain years;* thus the Clinical Society's Report points out that of the cases reported in the years 1869-1880 (inclusive) forty, or nearly 70%, occurred in the three years 1874-76. Garrod, on the other hand, mentions (15)[2] that only one case of hyperpyrexia in rheumatism occurred in St Bartholomew's Hospital during the six years 1881-86. This question may possibly, however, have involved in it another one, viz., the influence of the *methods of treatment employed.*

The influence of treatment upon the occurrence of hyperpyrexia might show itself in two distinct ways:—(1) Undoubtedly cases of the condition *ought to* occur less frequently since its mode of onset has become so much more widely recognised; for, on the appearance of suspicious symptoms, hourly or even more frequent temperature records are now taken, so that prophylactic treatment may prevent the temperature rising to an excessive degree, and hence the percentage frequency of hyperpyretic cases should be diminished. (2) But apart from this direct prophylactic treatment of the condition, is it not probable that, as a result of the almost universal adoption of the salicyl compounds in the treatment of rheumatism, the tendency to hyperpyrexia will show itself less often? It is not my intention here to enter upon the question of the treatment of rheumatism, but it may, I think, be fairly assumed as proved that the action of these salicyl compounds in rheumatism is a *specific anti-rheumatic* one, in other words, that they destroy or antagonize the rheumatic poison. Now, since the continued presence and action of this rheumatic poison is (as we shall see later) believed to be one of the chief factors in the causation of hyperpyrexia in rheumatism, is it not a fair enough deduction that the more rapidly the action of this poison is checked the less likely will hyperpyrexia arise? In this connection it is

[1] p. 264. [2] p. 45.

noteworthy that, according to most investigators, the onset of hyperpyrexia is most liable to manifest itself in the *second week* of the fever. Thus Bryant (dealing with sixty-seven cases in which information on this point was given) found (3) that 47·8% of these cases of hyperpyrexia occurred during the second week of the rheumatism, the first week showing only 19·5% of the cases. But under our more modern methods of treatment of rheumatism, the pyrexial process as well as all the symptoms of the disease are usually completely checked within the *first* week, so that if the amount and especially the duration of the pyrexial process in rheumatism are important factors in the production of hyperpyrexia then our more rapid methods of terminating this process *ought to* result in a considerable reduction in the number of hyperpyrexial cases in rheumatism.

Whether there may be any influence of *locality* or *race* has not, so far as I know, been shown, but an examination of the statistics of the medical wards of the Edinburgh Royal Infirmary as published in the Edinburgh Hospital Reports, would suggest that cases of hyperpyrexia are not very common in that institution. I found only one case mentioned (12) as occurring during the four years 1892-95. By the kindness and courtesy, however, of the medical registrar, Dr Lockhart Gillespie, I am enabled to give a table of statistics, not only more complete, but also extending over a longer period, viz., eight years (1889-90 to 1896-97), which brings out the fact that there were in all seven cases during that period. As shown by the table subjoined, this gives a percentage frequency of hyperpyrexia to the cases of rheumatism of ·64%, the total number of cases of rheumatism on which it is based amounting to 1075.

TABLE OF CASES OF RHEUMATISM AND OF HYPERPYREXIA IN THE ROYAL INFIRMARY.

Year. Oct. 1. Sept. 30.	Total Admissions.	Case of Acute and Sub-acute Rheumatism.	Cases of Hyperpyrexia.
1889 - 1890	3530	103	0
1890 - 1891	3887	82	1
1891 - 1892	3776	59	3
1892 - 1893	3944	107	0
1893 - 1894	4078	181	0
1894 - 1895	4689	168	1
1895 - 1896	4440	189	0
1896 - 1897	4546	186	2
	Totals	1075	7

Thus when fuller statistics are dealt with, the percentage

frequency of hyperpyrexia in the Royal Infirmary of Edinburgh is brought out as apparently just about the average, but owing to the ambiguity attaching to the term "hyperpyretic" temperature it is possible that some of these cases do not properly come within the category adopted in this paper,—one such indeed will be referred to later on in another connection.

I have not been able to find any information regarding the frequency of hyperpyrexia relative to the cases of rheumatism in *warmer climates* or amongst *foreign races*.

It is thus evident that it is very difficult to give even a fairly approximate idea of the frequency of the occurrence of this complication. The percentages which have been given vary from ·38 (Bryant's) to nearly 1·7 (cases in Middlesex Hospital as in the Clinical Society's Report); while it is impossible to draw conclusions from totalling the various published statistics because the observers have often chosen quite a different temperature as the hyperpyretic limit.

II. *Age.*—Allusion has already been made to the influence that the age of the rheumatic patient has upon the question of the occurrence of hyperpyrexia. Its greater prevalence in adults and especially between the ages of twenty and thirty is brought out by all investigators. Thus the Clinical Society's Report shows that 43·3% of the total of hyperpyrexial cases occurred in this decade, while Bryant, with slightly larger statistics to work upon, brings out practically the very same result—44·4%. This is also the decade at which the prevalence of rheumatism appears to be about its maximum, the Collective Investigation Report giving (8)[1] 34·8 as its percentage of 655 cases, but the possible vitiation of the averages through the scantiness of the reports of rheumatism amongst children must be allowed for.

Nothing is more striking in dealing with the question of the influence of age upon rheumatic hyperpyrexia than the unanimity with which authors refer to its absence in rheumatism in *children*. Practically every writer on children's diseases speaks of this, the chief source of immediate danger in acute rheumatism, as unknown in children. In his article on Rheumatism in Keating's "Cyclopædia of Children's Diseases," *Cheadle* (5)[2] says: "The temperature seldom runs high, rarely above 102° or 103° (except in older children). . . . This is the more notable, because it is at variance with the general rise of temperatures in childhood, which tend to be more easily raised and to range higher than in later life. And as anything like high temperature is rare, fatal hyperpyrexia is unknown, and one element of immediate danger is wanting." Similarly, writing at a more recent date, the same authority (6)[3] says: "I have never seen

[1] p. 387. [2] p. 797. [3] p. 42.

an instance of excessive or fatal hyperpyrexia in a child, nor any case in which the temperature has shown a persistent tendency to run up rapidly beyond control to a fatal height."

Donkin (10)[1] says: "Hyperpyrexia is very rare; I have met with but one probable and seemingly well-marked case of the so-called cerebral rheumatism of childhood, a necropsy, however, which might have definitely excluded other diseases being unobtainable."

Similarly *Henoch*, notwithstanding his vast experience, mentions (18)[2]: "I have as yet seen just one case of the so-called cerebral rheumatism such as has been observed in adults . . . and in this case chorea set in simultaneously and death ensued from pericarditis;" while the condition is not so much as even mentioned in *Emmett Holt's* recent work on children's diseases.

Garrod in his treatise has this statement (15)[3]: "The grave form of cerebral disturbance which is accompanied by hyperpyrexia is unknown in earlier childhood"; and *Bryant*, in his list of eighty-three cases of rheumatic hyperpyrexia, has no instance under the age of ten (quinquennial periods not given). The earliest age at which I can discover any case occurring is one of a boy of ten, though no mention is made of the height the temperature attained. Dr *Barlow*, who reports the case (1)[4], says that amongst other phenomena, "for two days there was hyperpyrexia," peri- and endo-carditis being found at the necropsy. This case is really mentioned in reference to the occurrence of *chorea* as a part of the rheumatic process in children. In the same paper he mentions another case of a girl of thirteen, in whom, after a train of rheumatic manifestations, fatal hyperpyrexia supervened (no temperature stated). In connection with the reference made by Barlow and by Henoch to chorea, it is noteworthy that *Marfan*, in the article on Rheumatism which he contributes to Grancher's "Traite de Maladies de l'Enfance" (21)[5], quotes H. Roger to the effect that "chorea is clinically the almost essential accompaniment of cerebral rheumatism in children, if it is not actually the symptomatic expression of it. I have never seen the one without the other." Marfan also refers to the comparative absence of the hyperpyretic condition in rheumatism in children —"Le rheumatisme cérebral proprement dit est très rare chez les enfants."

The interest of this absence of hyperpyrexia in rheumatism in children will be further brought out when the question of the etiology of the condition is under discussion.

III. *Sex.* — This has a very marked influence upon the incidence of the complication. Bryant's statistics bear out only more strongly the conclusion arrived at by the earlier report of

[1] p. 212. [2] p. 359. [3] p. 75. [4] p. 513. [5] p. 499.

the Clinical Society that *males* show a much greater proclivity to rheumatic hyperpyrexia than females, the percentages being shown in the following table:—

	Hyperpyretic cases.	Cases of Rheumatism.
Males .	58 or 70% (about)	654 or 50·3%
Females .	25 „ 30% „	646 „ 49·7%

The parallel column of figures is taken from the Clinical Society's Report founding on 1300 cases of rheumatic fever, in which the incidence of the disease upon the two sexes was shown (7)[1] to be almost equal, thus emphasising all the more the greater prevalence of hyperpyrexia amongst *male* rheumatic patients.

IV. *Heredity.*—There has not been any very definite evidence brought forward to indicate that patients who show an *inherited tendency to rheumatism* are more apt than others to exhibit hyperpyretic symptoms. The proportion of the hyperpyretic cases in the Clinical Society's Report who showed inherited rheumatic tendencies, was just about the same as that of the ordinary cases of rheumatism. Moreover, the difficulty of obtaining satisfactory family histories from many hospital patients renders deductions based on such investigations comparatively valueless.

As regards the question of the influence of heredity in another direction, viz., so far as concerns the presence or no of *neurotic proclivities* in the patients who develop hyperpyrexia, I have not been able to obtain any mention in the literature I have been able to examine. We shall see later that one factor which is supposed to have influence in producing the condition is an unusual susceptibility of the nerve-centres, and such a condition one might naturally look for in those with a tendency to instability of their nervous organisation. No mention is made in the Clinical Society's Report of evidence of the existence of such inherited tendencies.

Rather an interesting point is alluded to in the Collective Investigation Report, in which, out of the four instances of hyperpyrexia recorded, two were those of a *father and son* of the same family. I have not been able to discover any parallel instance amongst the various published records to which I have had access.

V. *Number of the Rheumatic Attacks.*—As regards the influence that this fact has upon the occurrence of hyperpyrexia, investigation has shown that *first attacks* of the disease are distinctly more liable to exhibit this phenomenon, a point in which the case of A. P. is thus not typical. Bryant found forty-six out of sixty-eight cases of hyperpyrexia (in which this

[1] p. 265.

information was given) occurred in *primary* attacks of rheumatic fever, a percentage of fully 67%. That this predominance of the complication in primary attacks is not simply due to the larger number of rheumatic patients in hospital suffering from the disease for the first time is made clear by examining the table given by the Clinical Society's Report, which shows (7)[1] that out of 1281 cases

52·7% were first attacks of rheumatism ;
30·5% „ second „ „ „
10·7% „ third „ „ „

Whether those patients who have had rheumatic hyperpyrexia are more liable to a *recurrence* of the condition in subsequent attacks of rheumatism is a point upon which I have been quite unable to get any information. Certainly I cannot find, after careful examination of the records of the eighty-three cases given by Bryant (in that portion of his paper which deals with hyperpyrexia in rheumatism) a single instance mentioned of hyperpyrexia having occurred in the previous attacks of rheumatism in the case of those who exhibited this phenomena in their second or subsequent attack. I have endeavoured to amplify the list of recorded cases given by Bryant by collecting, so far as I could, the cases published in various journals between the date of his paper (1892) and the present year[2]—eleven in all, which, when added to the five instances which have occurred in Leith Hospital (all unpublished), brings the total to ninety-nine cases ; and yet, out of this large number, there is *only one example* of the *recurrence of rheumatic hyperpyrexia in the same individual.*

As regards cases occurring before the method of treatment became generally adopted which is so frequently successful nowadays, no doubt the mortality was so great that probably few of the "first attack" hyperpyretics survived to run the risk of a subsequent attack. But with the death-rate considerably reduced as it is now, owing to the almost universal employment of cold in the treatment of this grave complication, it *should* be possible to collect sufficient records of subsequent attacks of rheumatism in the survivors of hyperpyrexia to show if the complication tends to recur in the same individual. I am glad that it is amongst the *five original* cases which I am able to record in this paper that an instance of this recurrence of hyperpyrexia in a subsequent attack of rheumatism in the same patient occurs. On the first occasion he came under my care when acting as house-physician at Leith Hospital in 1889 (three weeks after the case of A. P., described in the beginning of this paper) ; while his second attack of hyperpyrexia occurred when he was

[1] p. 266. [2] 1898.

again under treatment in Leith Hospital in 1894, the notes of the second attack being extracted from the hospital records, while those of the former are from my own memoranda taken at the time. Briefly, the notes of the two attacks are as follows:

CASE II.—A. S., aged thirty-five, had been ill with (apparently) his second attack of rheumatic fever for about a week. Dr Wm. Stewart (who kindly furnished me with some of the details of the case) was suspicious of some impending mischief from the fact that his temperature did not fall under the ordinary salicyl treatment, and he asked me to admit him as he feared the onset of hyperpyrexia, saying that while he could not state definitely what led him to form this opinion, there was something in the patient's look and manner which was unusual in ordinary rheumatic fever. When admitted to Leith Hospital on November 9th, 1889, his temperature in the forenoon was 101·4°, and though in the evening it rose to 103·6°, there was nothing special to be noticed as unusual in a moderately severe attack of acute rheumatism. Next morning, however, his temperature (which was being frequently taken) was 104°, and remained so in spite of antipyrin gr. xxx. (two doses of gr. xv. with forty-five minutes' interval). A large icebag was then applied to the abdomen, but in spite of this the temperature suddenly rose to 106·2°, the patient passing rapidly into a state of coma. A general icepack was immediately applied to the whole body and continued for twenty-five minutes, by which time the temperature had fallen to 102·2°. The patient was then removed to a dry bed and covered with a light blanket, the temperature continuing to fall to 98·8°; he was now conscious and able to swallow the brandy and digitalis which were administered four-hourly for some time. By 10 P.M. the temperature had slowly risen again to 103·8°, when quinine sulphate was commenced, gr. iii. being given hourly for six doses, the temperature showing no sign of rising higher. The after-progress of the case need not be detailed further than to say that the temperature slowly but steadily fell, and was normal by the sixth day after the onset of hyperpyrexia.

CASE III.—A. S., now aged forty, was again admitted to Leith Hospital on October 6th, 1894. I am unfortunately unable to produce a copy of the temperature chart of this attack, but the Hospital record states:—"Present illness has lasted three weeks; pains most marked in knees, but also in wrists. Tongue very dry; bowels not acted for four days. No cardiac murmurs or friction. Treated with sod. salicyl. gr. xv. every hour; tr. digitalis ℥ v. every four hours."

October 7th.—"Pains almost away. Salicylate to be given hourly till bed-time, then two-hourly."

October 8th (Morning).—"Deafness present: no pains: little sweating; salicylate every two hours during the day. (Even-

ing).—Temp. rising, at 6 P.M. 102·6°, at 11 P.M. 104°. No pain; 'wandering' slightly; very restless. Stop salicylate. Morphia gr. ⅓ given hypodermically. Slight friction detectable at base of heart: blister applied. Temperature to be taken every fifteen minutes."

October 9th.—"At 1.15 A.M. temp. 105·4°, pulse 88. At 1.30 A.M. temp. 106·2°. Patient at once put into a bath, and in twenty-five minutes his temperature fell to 99·2°, when he was immediately removed; but marked collapse followed, with a temperature persistently at 95° for nearly an hour and a half, and a pulse rate of 44 per minute. Vigorous and persistent friction, with brandy and ether hypodermically, and the application of mustard and hot cloths to the precordia and abdomen were persevered in, and the patient gradually rallied, his temperature at 4 A.M. being normal. His temperature never again rose above 104°, ice-bags being employed for a time to the head and abdomen; and in spite of more than one relapse of the rheumatism and a pericardial effusion which appeared a fortnight after his hyperpyrexial attack, he made a satisfactory recovery and left cured on December 13th, 1894."

It is, I think, interesting to note that A. S. has *again* been in Leith Hospital under my care for another sharp attack of acute rheumatism in March 1897. His temperature was 102·6° on admission, but he reacted to salicyl treatment rapidly, and made a speedy recovery without the slightest tendency to hyperpyrexial symptoms.

VI. *Character of the rheumatic attack.*—Before passing on to consider the characteristic features of hyperpyrexia, one other point in reference to its occurrence calls for notice. The phenomena is by no means confined to severe attacks of rheumatism, on the contrary, the condition frequently arises in *mild* cases of the disease from which, I think, the valuable conclusion follows that we should never neglect to follow systematically the course of the pyrexial process in even slight cases of rheumatism. A case which occurred while I was an assistant in private practice appears to me to illustrate the importance of this.

CASE IV.—E. H., a servant girl, was seen at home by her doctor, who found her complaining of merely vague pains, like those of slight sciatica, in the region of one hip. Her temperature was at that time *normal.* Considerable delay occurred before the patient arranged to go into Leith Hospital, and on her admission there, forty-eight hours after being first seen, her temperature was found to be 105·8° and she was in a state of slight delirium which gradually increased up till death, which occurred in fifty hours, although her temperature never again rose to 105°. There was distinct effusion in one knee on ad-

mission, and there can be little doubt, I think, that she was suffering from acute rheumatism.

But apart from its occurrence in mild attacks of rheumatism hyperpyrexia may ensue when the patient is convalescent from the disease and apparently perfectly well, as in the well-known case reported by Ringer in 1867—that of a young woman who, having been convalescent for some time, was to leave hospital on the following day when her temperature suddenly rose to 110°, and she died within a few hours. Thus it is evident that at any period in an attack of rheumatism the formidable condition of hyperpyrexia may present itself, but it would appear that it most frequently occurs, as already noted, about the *second week* of the disease.

Symptoms and Mode of Onset.

The mode of onset varies considerably. In some instances it is insidious, little being present to suggest that the patient is on the verge of a dangerous condition until this fact is suddenly revealed by the occurrence of violent delirium or a convulsion; or again, as in the case of A. P. recorded above, it may be only when the temperature is taken in the usual routine that the startling fact is disclosed. If the case has been a severe one, the temperature may have been for some time maintaining a high level, little influenced by the salicylates or other treatment adopted; but, as already stated, the previous pyrexia may be of quite moderate degree. Still, should the temperature in a case of true rheumatism continue to show little sign of declining, in spite of regular and sufficient doses of the salicyl compounds, the onset of hyperpyrexia is always to be feared.

As an illustration of this, I may append a brief record of another case of rheumatic hyperpyrexia occurring in Leith Hospital, of which, unfortunately, I am unable to reproduce the temperature chart, but the following short note contains the salient features of the case:—

CASE V.—H. N., native of Shetland, domestic servant, strong and robust, but "very nervous about herself," was admitted to Leith Hospital on October 21st, 1893, with a severe attack of rheumatic fever. Profuse sweating. Temperature, which was about 102°, was practically unaffected by repeated doses of the salicylates during several days, and she became worse, the temperature on the seventh day after admission rising to 108°, with accompanying coma. She died a few hours later, no treatment for the hyperpyrexia having been employed in the case further than cold sponging.

One symptom, however, is especially to be remembered as a danger signal to put us on our guard—I refer to *delirium*. This is probably the most frequent *precursor* of hyperpyrexia,

as it is also the most constant *accompaniment* of its onset. No doubt it is also a symptom frequently present in *pericarditis*, and may be an evidence of the supervention of *this* complication in the disease; but the appearance of delirium even when pericarditis is present, and still more when no evidence of this can be discovered, should always lead to the greatest vigilance on the part of the patient's attendants, so that any further development, especially in the course of the temperature, may be noted at the earliest opportunity. Another explanation which is given sometimes of the onset of delirium in cases of acute rheumatism is the action of the salicylates. While no doubt it is true that, in certain individuals at least, the administration of these drugs, even in comparatively small doses, is followed by evidences of cerebral disturbance, and especially delirium, still such an explanation of the presence of this symptom should not be too hastily adopted without the greatest care being taken to eliminate the possibility of the other and more formidable cause—hyperpyrexia—being at the root of the matter.

Amongst other symptoms which occasionally usher in the condition is *insomnia*, which may be rather pronounced, and a restlessness on the part of the patient, but on the other hand there is instead sometimes a drowsiness which gradually deepens into fatal coma.

Headache or a feeling of malaise is by no means frequently complained of. On the contrary one of the most striking phenomena is that the patient frequently has almost entire *cessation of joint pains*. This relief from his previous articular symptoms was well-marked in the case of A. P. which I first narrated, when the patient was so satisfied with the improvement (as he thought) in his condition that it was with the greatest difficulty he was got to realize the dangerous condition he was in, although his temperature even then was 107°. That the relief from joint pains in his case meant more than a mere dulling of his sensory functions from commencing unconsciousness is, I think, evident from the fact that he was able to argue quite intelligently with his medical attendant regarding the necessity for his removal to hospital, although within half-an-hour thereafter he was profoundly comatose. While this phenomenon, then, is very characteristic of the onset of hyperpyrexia it is by no means constantly present; the Clinical Society's Report (7)[1] mentions that out of the cases in which information on this point is given cessation of joint pains occurred in 55·5%, but as nearly a third of the records were silent on this point it is probable that this overstates the per centage of cases illustrating this prodromal manifestation. Nevertheless the cessation of articular pains *without coincident fall in the temperature* should always

[1] p. 269.

give rise to a suspicion of a possible hyperpyretic condition ensuing, and lead to the greatest watchfulness in regard to the progress of the pyrexia, observations being taken half-hourly or even oftener.

Another change in the patient's general condition which has been observed, and has been frequently referred to in cases of hyperpyrexia, is the *cessation of sweating*. Bryant shows from his collected cases that this is far from being a constant symptom, his statistics bringing out (3)[1] the proportion of cases in which this occurs as about 25%, practically the same as that given in the earlier Clinical Society's Report ; but when it does occur, as in the case of A. P. very markedly, the pungent and dry condition of the skin (similar to that found in a severe case of scarlatina) is a very striking phenomenon in contrast to the usual moist and clammy skin of a rheumatic patient.

In one of the cases which occurred in Leith Hospital prior to the onset of hyperpyrexia a certain nervousness on the part of the patient with an apprehension of a fatal termination to the illness was very marked, and I have found the same condition noted in some of the published cases.

Another symptom which has been described as preceding the onset of hyperpyrexia occasionally is excessive micturition, the urine being pale and of low specific gravity, but with this, as in the case of the cessation of perspiration and the disappearance of joint pains, their occurrence is rather *coincident with* than *prodromal of* the hyperpyretic state, the chief premonitory manifestation being delirium, and to a decidedly lesser extent the continued pyrexia uninfluenced by treatment. In some instances the delirium also is *merely coincident with* the hyperpyrexia in its onset, and in a few cases even does not set in till *after* this; but the majority of the recorded cases show it to have been present prior to the rise of temperature. In connection with this it may be noted that the Clinical Society's Committee record the fact that this early onset of delirium apparently denotes a severe type of hyperpyrexia, the proportion of fatal cases being unusually high when this was the case (7).[2]

From a study of the temperature charts of the cases under their consideration they also described (7)[3] five types of hyperpyrexia, not only as regards its mode of onset, but also its progress, and although many cases present features of more than one group, these types may be shortly alluded to.

I. In some cases the temperature after rising gradually for a few days suddenly culminates in a maximum by an exacerbation of several degrees. (Perhaps the patient A. S. in Case II. might be taken as an illustration of this type.)

[1] p. 401. [2] p. 271. [3] *Ibid.*, p. 273 sqq.

II. In others "the temperature, after maintaining for one or more days a moderate level, suddenly rises to excessive heights." (Of this class in one respect A. P., Case I., was certainly an instance.)

III. Another type described is "that of a pyrexia of a more continuous course, not unlike that of typhoid without violent or excessive exacerbations." (The cases under this head would probably not be admitted into the hyperpyrexial category by some observers, *e.g.* Bryant, the maximum temperatures having been 105°, 105·6°, and 105·8° in the three cases of the group.)

IV. Here the temperature rises "gradually to a maximum, and is then permanently reduced by the cold bath or wet pack."

V. This group comprises "cases of severe character in which the tendency to rise to hyperpyrexial heights is very pronounced, so that to control it cold baths have to be frequently repeated." (Possibly Case I., A. P., belonged really to this type.)

To sum up this part of our subject, then, the typical clinical picture of a case of rheumatic hyperpyrexia might be thus described. A male, of about thirty years of age, in the course of a moderate attack of rheumatism, begins, probably about the end of the first week of his illness, to suffer from delirium, and may become restless; his sweating diminishes (often suddenly), while his articular pains cease, so that to his friends he may appear to be improving, when, frequently without further warning, a convulsive seizure or a stuporose condition supervenes, which, unless promptly treated, soon passes into fatal coma with the cyanosis and stertorous respiration so frequently seen in grave cases of cerebral apoplexy.

THE PATHOGENESIS OF RHEUMATISM AND THE THEORIES AS TO THE PRODUCTION OF HYPERPYREXIA IN RHEUMATISM

BEFORE passing on to consider the theories as to the production of hyperpyrexia, it will be advisable first to enquire into the views which are entertained as to

The Pathogenesis of Rheumatism,

in order that we may see whether any light is thrown on the nature of the hyperpyrexial process by a consideration of the pathology of rheumatism.

Prior to the time of Sydenham, rheumatism and gout were not in this country at least recognised as separate diseases; but ever since he differentiated the two maladies, speculations have been numerous as to what the real nature and causation of rheumatism might be. More or less satisfactorily each theory tried to account for the various peculiarities associated with the disease—the apparent influence of heredity, the apparent connection of chills or cold and damp with the onset of the malady, and the tendency to subsequent attacks of the disease in the same patient as well as relapses during its course. To each of the various theories propounded on the subject objections have been urged, so that the problem of the *nature of the morbid process* of rheumatism is by no means so settled as is the *clinical* question of the *method of treatment.* Briefly stated, the chief theories relative to the pathology of rheumatism have been as follows.

The Nervous or Neurotic Theory.

According to this hypothesis, which in this country numbers amongst other supporters Buzzard and Hutchinson, the source of the arthritic troubles (regarded by its advocates as the chief or essential items in rheumatic fever) is believed to lie in a *disturbance of the centres for nutrition of the joints* situated in the central nervous system, probably in the medulla. This disturbance is said to arise from *peripheral irritation* applied to the cutaneous nerves, the *consequence of a chill.* Those who advocate this theory are influenced by the well-known pathological fact of the occurrence of joint troubles arising from lesions of nerves or the central nervous system, *e.g.* Charçot's joint lesions in

Locomotor Ataxy, and point to the condition termed *Rheumatoid Arthritis*, which is now generally assumed to be essentially a *trophic* disturbance of joints. Buzzard further suggests that the *excessive sweating*, so characteristic of rheumatism, may arise from a similar disturbance of the sweat-centres, which are believed to lie in the medulla in close proximity to the supposed centre for nutrition of joints; while the hyperpyrexia which occasionally occurs has similarly been attributed to a corresponding affection of the heat-centres. But, as has been pointed out by Maclagan (20),[1] the *type* of acute inflammation present in rheumatic fever is perfectly different from the form of joint affections which occurs as the result of trophic disturbances in certain diseases; and, moreover, the arthritis is only a part of the rheumatic process; no explanation is given by this theory of the *visceral* lesions so frequently present and so strikingly characteristic.

Latham brought forward a modified form of this "nutrition" theory, the essential of which is that the impaired action of the centres was brought about by irritation from *chemical products* (uric and lactic acid) resulting from an *alteration in the metabolism of muscles* consequent on the hyperoemic condition produced in them by the "chill." This "*Neuro-Chemical*" theory may be considered as partly allied to the following, which was for long the most widely accepted view.

The Lactic Acid Theory.

Though the hyperacid condition of the urine, and the excessive and acid sweats of acute rheumatism had been noticed long before his time, Dr Prout was apparently the first to suggest that the materies morbi might be found in the excess of lactic acid, which was stated to be present in the blood in acute rheumatism. Various modifications of his original suggestion have been put forward; in its most modern form the theory may be thus shortly summarised:—Lactic acid is the product normally of muscle metabolism; it is formed in greater quantity during exercise, but this increased formation is compensated for by its increased elimination (in the form of carbonic acid and water) in the greater activity of the lungs and skin as the result of exercise. Hence the usual balance between production and elimination is maintained. Should, however, the increased eliminative action of the skin be interfered with, *e.g.* as the result of a chill to the surface of the body, then lactic acid accumulates in excessive quantity in the blood and acute rheumatism results.

Around this view a warfare has long waged. Apart from

[1] p. 219.

the statement made by Garrod (15)[1] that "there is no evidence of any excess of lactic acid in the blood of rheumatic patients," it is evident that the theory is faulty in several points, to mention only one—the impossibility of such an excess of lactic acid being produced as the result of even severe exercise as to account for the increased elimination lasting frequently for weeks. It has been urged in its support that (1) inflammatory changes similar to those of acute rheumatism have been produced in dogs by the injection of lactic acid into their system, and (2) that the administration of lactic acid has produced symptoms in man indistinguishable from those of rheumatic fever. Much interest was naturally aroused by these apparently confirmatory proofs of this popular theory of rheumatism; but it is stated by Maclagan (20)[2] that Reyher has shewn the so-called "Endocarditis," which Dr Richardson ascribed to the irritation of the lactic acid injected into dogs, to be a condition which is not pathological at all but is found in dogs irrespective of the cause of death; while the evidence adduced by Foster from the administration of lactic acid to diabetic patients when carefully analysed merely shews (20)[3] that the results of such administration are increased action of the skin, and "failing this, disturbed nutrition of, with consequent pain in, the muscles and the fibrous textures of the joints." Thus while the presence of lactic acid may and probably does account for some of the *symptoms* of acute rheumatism, it cannot be finally accepted as the *cause* of the condition; in reality it is one of the phenomena of the disease and its presence throughout its course has itself to be accounted for.

It was only to be expected that rheumatism, as in the case of so many other diseases, should be ascribed to the entrance from without of some organismal poison. The various manifestations of the disease might thus be explained as the results of the toxines produced in its course. There is practically no evidence that it is distinctly infectious or contagious in nature, but its resemblance in many points to pyœmia could hardly fail to suggest an *infective* process as its cause, but as yet bacteriological research has failed to demonstrate any micro-organism as the specific cause of acute rheumatism. Many investigators have been for long cultivating this field of study, but in support of the view that this disease has many affinities with other infective processes, the researches of Dr Newsholme of Brighton especially call for at least a passing notice. In the Milroy Lectures for 1895 (22),[4] as the result of a most painstaking examination of a vast amount of material, not only on the subject of the periodical occurrence of special outbreaks of rheumatism at certain times (the proof of which he largely draws from the returns of notified cases of acute rheumatism in Norway, Sweden,

[1] p. 22. [2] p. 209. [3] p. 216. [4] p. 589 *sqq*.

Denmark and other neighbouring countries in which this disease has been compulsorily notifiable for periods varying from fifteen to thirty years), but also from enquiries instituted especially into the connection that appears to exist between the occurrence of cases of rheumatism and the *state of moisture* of both the *atmosphere* and the *soil*, he arrives at conclusions which may be thus briefly formulated:—

(*a*) Rheumatic fever is the result of the multiplication in the system of a *pathogenic micro-organism*;

(*b*) That this organism is probably *saprophytic* with a tendency to *parasitism*; and

(*c*) That in *dry* years, associated with *low ground water* and *a high soil temperature*, the growth of this organism is so favoured as to give rise to outbreaks of acute rheumatism which are practically *epidemic*.

There is no need to do more than merely mention the suggestion of Friedlander who, combining the idea of an "infective" process with the former "nutritive" theory, put forward the somewhat original proposition that acute rheumatism is but one of a group of various diseases (*e.g.* exophthalmic goitre, diabetes, &c.) which he calls *central rheumatism*, the cause of which is to be found in a central medullary lesion, which is in turn produced by a specific micro-organism.

Nor need we be detained by considering the theory of *Hueter*, who, regarding endocarditis as the first link in the chain of events, suggested that this was produced by the entry of an organism from without, and that the joint lesions were the result of endocardial embolisms, though the micro-organism itself might also take some part in their production. Since endocarditis, however, has been amply proved by autopsies to be frequently absent, the theory built on this foundation falls to the ground.

The view which has found most acceptance under the category of "infective," and which has in its support to a large extent the conclusions arrived at by Newsholme after his researches, is that which, founding on the similarity of rheumatism in many respects to ague and malarial diseases, is called the

The Miasmatic Theory.

There is no need to enter here upon an examination of the many points brought forward in support of this view by its most prominent advocate, Dr Maclagan. It will suffice to give merely a brief summary of his theory, which is essentially this, viz., that for the production of rheumatism there are *two factors* necessary—(1) a *poison* (which he regards as in some respects analogous to that of ague) which enters the system from without and finds in certain people the (2) *nidus* essential for its vivifica-

tion and reproduction. This nidus he regards as occurring in the fibrous and serous tissues of the motor apparatus. In his own words (20) :[1] "The poison of rheumatic fever is a miasmatic organism which is propagated in the system and finds the nidus requisite for this propagation in those fibrous and serous tissues of the motor apparatus whose inflammation constitutes the special lesion of the disease." In the light of this theory he has discussed at great length the many and varied phenomena of the disease, maintaining that (1) the hereditary tendency to the affection consists really in the *inherited peculiarity of tissues* containing the requisite nidus ; (2) that the excessive perspirations are the result of the greater formation of lactic acid from the *increased muscle metabolism*—muscle being one of the chief seats of the nidus ; (3) that the intracardial lesions, in their particular anatomical sites on the left side of the heart, are really at the outset essentially lesions of the *fibrous tissue* and not primarily of the endocardium proper ; while (4) the success of the treatment which he introduced, to this country at least, is ascribed to the direct *antagonistic and destructive action of the salicyl compounds* upon the first of the two factors in the disease —the poison,—relapses or recrudescences arising through the antidote having been cut off before all the poison in the system has come under its power.

While accepting, then, this miasmatic theory as perhaps the most probable hypothesis yet put forward to account for the phenomena of rheumatism, there is one point I would specially remark on in reference to Maclagan's comprehensive discussion of this subject, namely the view which he seems to take of rheumatism as being essentially a disease which occurs *after* childhood ; as he says (20)[2] : "The age of liability to rheumatic fever is from fifteen to fifty," and again,[3] (It is) "rare before fifteen," ; while in another part of the same work, when speaking of the hereditary predisposition, he uses these words:[4] "This inheritance seldom declares itself before fifteen." Scarcely sufficient attention is paid in his writings, it seems to me, to the amount of evidence which has been brought forward in recent years by Barlow, Cheadle and others of the undoubted fact that acute rheumatism is far from an uncommon disease in children, though no doubt its manifestations in childhood do not usually present quite the same type as in persons over fifteen. I draw attention to this point, not because it at all weakens, so far as I can judge, his arguments, but because the application of Maclagan's miasmatic theory to the explanation of the *rheumatism of children* may possibly help to throw a little further light on the question we have next to consider, viz., the *production of hyperpyrexia.*

[1] p. 234. [2] p. 232. [3] *Op. cit.*, p. 201. [4] *Op. cit.*, p. 234.

Pathogenesis of Hyperpyrexia.

Before we can take up the subject of the pathogenesis of rheumatic hyperpyrexia and the theories regarding it, a brief résumé is required of the views at present entertained as to the means by which—(*a*) the *normal* body-temperature is maintained, and (*b*) the condition termed *pyrexia* is brought about.

(*a*) Normal Temperature Mechanism.

The thermal apparatus of the human body is believed to consist in the following:—(1) *heat-producing* structures; (2) *heat-eliminating* structures; and (3) a *controlling nervous centre* in communication with both of the preceding. Heat is universally admitted to be produced by tissue metabolism in all parts of the body, the chief seats of this being the skeletal muscles and the liver. The heat so produced is got rid of by several channels—the lungs, kidneys, &c., but for practical purposes chiefly through *the skin*, both by radiation and the evaporation of sweat. Thus Vierordt's experiments show (24)[1] that 87·5 % of heat loss is effected through this channel alone. To ensure a proper balance being maintained between production and elimination, it is essential that there be some controlling mechanism, and Macalister in his Goulstonian Lectures for 1887—as quoted by Hale White (16)[2]—suggested that it consisted of the following:—(1) "A *thermolytic* mechanism, acting chiefly through the skin by the cutaneous vessels and the sweat glands, having its nervous centre in the *medulla*; (2) a *thermogenetic*, consisting of—(*a*) the muscles, or (*b*) that part of the cerebral nervous system—probably the corpus striatum—which controls this function of muscles, and (*c*) nervous paths connecting these two; (3) a higher controlling or *thermotaxic* mechanism whose office is to adjust the balance between the other two." When, therefore, *e.g.*, during severe exercise the increased tissue metabolism of the muscles necessarily results in a large augmentation in the heat of the body, the temperature is kept from rising by a counter-balancing increase in the heat loss, which accompanies and follows the exercise, manifested by the glowing and perspiring skin of the athlete. The precise localisation of the seat of this thermotaxic nervous mechanism is unknown, though Hale White in the same article (16)[3] suggests that "probably we should look for it in the cortex." Ott, who has shown that[4] "when putrid blood is injected into the veins, it is impossible to produce fever (in animals) if the corpora striata have been removed," also states further (23),[5] on more or less satisfactory data, that "in the lower animals *six*

[1] p. 850. [2] p. 467. [3] p. 468. [4] *Op. cit.*, p. 473. [5] p. 434.

centres have been localised, injury of which causes increased temperature, viz.—(1) the cruciate at the rolandic fissure; (2) part of the sylvian; (3) candate nucleus; (4) tissues about the corpus striatum; (5) anterior and inner end of the optic thalamus; and (6) a point between this latter and the corpus striatum." It is only right to mention that in the most recent work on physiology (published since the foregoing was written) Pembrey (24)[1] evidently regards the proof as to even the existence of heat centres as insufficient, his summary being stated thus —"an impartial examination of the above evidence leads to the verdict that the existence of the so-called heat centres in the brain has not been proved." But in any case the correctness of Ott's anatomical localisations does not materially concern us here. The brief sketch given above of the three mechanisms may suffice for our present purpose, and enable us to pass on to consider

(*b*) The Pyrexial Process.

If the mechanism for heat regulation be such as above described, pyrexia or elevation of the body temperature above normal might *theoretically* be produced in either of two ways—(1) from an increased heat production, or (2) diminished heat loss. The exact nature of the process has been the subject of much investigation, but briefly it may be stated that (largely as the result of Dr Hale White's elaborate experiments and observations) it is now generally admitted that in all probability the febrile process (whereby pyrexia results) is *not the same* in all cases. *Each* of the two *theoretical* types of pyrexia probably occurs. Thus Dr Hale White, after giving the results of an interesting series of investigations in various diseases, mentions (17)[2] that in some conditions (of which he gives enteric fever as an example) "the pyrexia in part at least is due to *diminished heat loss*," while in "others this is of but slight importance, and then the *production of heat is very great*," pneumonia being the ailment he takes as illustrating this variety of pyrexia.

Such being the most probable view of the process in *pyrexia*, the question naturally follows—is *hyperpyrexia* produced in the same way, or, in other words, is the *hyper*pyrexial process *literally* an "*exaggerated pyrexial*" process? This leads us to enquire whether all cases of hyperpyrexia appear to own the same cause, or whether the method of production varies in different diseases?

Now hyperpyrexia (or perhaps, in this connection, better "excessive temperature") is a condition exhibited in a great variety of diseases, and while no doubt in one sense all cases of *hyperpyrexia* are characterised by the same phenomenon, still is

[1] p. 865. [2] p. 1725 *sqq.*

there not something to be said in favour of regarding them—*clinically* at least—as showing more than one type?

1. In some cases the excessive temperature might almost be regarded as *merely an exaggeration* of the characteristic pyrexia of the particular disease. Thus in the case of a patient who has had for some days a severe attack of pneumonia with a high level of temperature probably reaching 105°, does not the rise of the temperature to such a point as 105·8° (*i.e.* beyond our so-called hyperpyretic limit) suggest a mere exaggeration of the pyrexial process in this special case? The fact (as above mentioned) of the pneumonic pyrexial process being essentially characterised by *excessive heat-formation*, is of itself somewhat significant in this connection.

2. In another group of cases the "excessive temperature" might be explained as being merely a *pre-mortem phenomenon*; by which I mean, that in the cessation of the vital processes this mechanism for temperature regulation is very markedly affected, if indeed it has not altogether ceased to act before the cardiac or respiratory mechanism has actually failed. In such cases death is, as it were, laying his hand early on this part of the organisation, just as it has recently been shown (11)[1] that in other instances respiration fails and ceases while the heart still goes on acting. May not the hyperpyrexia occasionally met with in *e.g.* tubercular meningitis be an instance of this pro-agonistic type, as it has been termed? That this variety at any rate is *universally fatal*, in contra-distinction very markedly to the previous type, will, I think, be admitted by all.

3. Another group of cases is formed by those in which the hyperpyrexia is produced by *an injury* to the cerebro-spinal nervous system. Surely *clinically*, as well as *anatomically*, there is a vast difference between the "excessive temperature" in the case of a man with cervical spinal injury or hæmorrhage into the corpus striatum, and the sudden temporary hyperpyrexia of an acute pneumonic fever or the pre-mortem rise of temperature in a meningitis.

That hyperpyrexia has not always the same grave significance and is probably not always produced in the same way is, I think, evident from the numerous well-authenticated cases of "paradoxical" or "hysterical" hyperpyrexia, none of which prove fatal, although the temperature rises far above limits which are fatal in other types.

Without pursuing this subject further, then, let us see if there be any variety of hyperpyrexia to which the form that occurs in rheumatism corresponds. There will be a general consensus of opinion that its analogue (and a very close one) is to be found in the condition described as *heat-apoplexy*, an affection in which

[1] p.

the patient (who has usually been previously in his ordinary state of health) is suddenly seized with headache, muscular pains, and a feeling of prostration followed by coma, with excessive temperature, which, unless treated, soon terminates in death. The resemblance between the symptoms of this condition and that present in rheumatic hyperpyrexia has been frequently commented upon; and (as Maclagan has shown) a consideration of the mechanism by which the excessive temperature is produced in *this* affection throws considerable light on the probable pathogenesis of rheumatic hyperpyrexia.

We have seen that in this latter affection there are other and frequently more prominent phenomena than the mere temperature elevation; the symptoms of nervous disturbance with a tendency to fatal coma are as essential parts of the process as the mere excessive temperature. Formerly it was supposed that these nervous symptoms were the *result* of the excessive temperature; but, apart from the fact that this in no way explained how the temperature alteration was produced, it is now quite well recognised that a patient may exhibit, even for some considerable time, a temperature of equally excessive limit and yet show no such "nervous" manifestations or tendency to coma and death, as *e.g.* in so-called cases of "hysterical" hyperpyrexia, or even relapsing fever (Maclagan). There is considerable reason for believing that the excessive temperature is the *result* rather than the *cause* of the nervous disturbance, and a study of the causation of the phenomena of heat apoplexy will probably best bring this out.

Heat-Apoplexy: its probable explanation.

If the normal *elimination* of heat be interfered with while the process of *heat formation* goes on uninterruptedly, it is evident that the temperature of the body must inevitably rise, and continuously so while life lasts, unless heat elimination is restored, or the heat production inhibited. Whether there exist separate centres—a "heat-inhibiting" and a "heat-producing" centre, with a still higher "heat-controlling" centre—or whether there be only one heat-controlling centre, with stimulating and inhibitory functions, has not been definitely proved. For practical purposes, what we have to deal with is the fact that the body-temperature may rise from two distinct causes—(*a*) stimulation of the heat-producing mechanism, or (*b*) inhibition of the heat-eliminating mechanism, while the temperature will similarly be reduced by reversing these processes. That this inhibitory function is an active and not merely a passive one is practically certain from the well-known fact that a "destroying" or non-inflammatory lesion of certain parts of the central nervous

system (*e.g.*, injury to the spinal cord in the cervical region, or hæmorrhage into the corpus striatum) is usually attended by a considerable rise of temperature, often to extreme limits. Now rise of temperature, as Maclagan points out, resulting from a destruction or a paralytic condition of part of the nervous system, can only mean that the normal function of that part was one of *active* inhibition. The analogous mechanism existing in the case of the heart is quoted by the same writer, where the vagus is constantly actively resisting the excito-motor mechanism, and so maintaining the pulse at its normal rate. But since heat (as we have seen) is the product of tissue-metabolism, *this* will be the process which requires to be kept within its proper limits by the inhibitory mechanism. Should this mechanism fail to act (through inhibition being paralysed), then the uncontrolled tissue-metabolism must inevitably produce hyperpyrexia. Such, then, is the explanation of the phenomenon of heat-stroke, which is brought about as follows:—The normal heat elimination of the body being interfered with owing to the high atmospheric temperature, the onus of preventing too much heat production is thrown upon the heat- (or metabolism) inhibiting mechanism, which, consequently, is kept acting at high pressure. Under ordinary conditions the mechanism is fit to cope with the difficulty, and nothing more serious than a sense of prostration and exhaustion results. But under certain circumstances the long-continued and excessive action of the heat-inhibiting mechanism results in its paralysis from over stimulation. *Heat-stroke* is thus held by Maclagan to be essentially a *fatigue paralysis of heat inhibition*, or, in a wider sense, a *paralysis of the inhibition of tissue metabolism.*

[Since the foregoing description of the present view of the pathogenesis of heat-stroke was written, an article on this subject has been published (25)[1] by Dr W. Sambon, in which he maintains the theory that the condition is due to a micro-organism, and that it is in short a "specific infectious disease." Consideration of his theory, and the arguments adduced in its support, would be quite out of place here; but I think it only right that the existence of another and contrary hypothesis should be noticed.]

Maclagan's Theory of Hyperpyrexia in Rheumatism.

Now the bearing of all this examination of the phenomenon of heat-stroke upon the pathogenesis of rheumatic hyperpyrexia is brought out by Maclagan in this way. The similarity between this condition and heat-apoplexy exists not merely in their symptoms and clinical features, as also the *post-mortem* appearances in fatal cases, but is emphasised by the fact that the same

[1] *The Etiology of Sunstroke*, Sambon. *Brit. Med. Journ.*, i., 1898, p. 744.

method of treatment succeeds in both conditions. Such a resemblance throughout naturally suggests that the phenomena are similarly produced in the two cases. The train of reasoning he pursues is as follows:—

1. *Tissue metabolism (of muscle) occurs to a greater extent in rheumatism than in any other febrile process.*—The *proof* of this he finds in the excessive quantity of lactic acid (the product of muscle metabolism) present in rheumatism, and which he states to be present in no other fever. The *explanation* of this abnormally excessive metabolism lies in the fact that the propagation of the rheumatic poison occurs chiefly in muscle which contains its nidus.

2. Granted, then, that muscle metabolism is excessive *in rheumatism*, it follows that *heat-production is also excessive*; in proof of which contention he again points to the extremely active condition of the skin (showing the compensating heat eliminating functions to be exceedingly active). If these balance each other, no undue pyrexia will result.

3. But while heat elimination is thus active, *the inhibitory mechanism will be in constant action upon muscle metabolism*, and in view of the excessive quantity of heat liable to be produced, this inhibitory mechanism *will be stimulated to work at high pressure.*

4. If, then, "*either from want of vigour, or from unusual susceptibility of the nerve centres, aided possibly by more or less failure in the heat eliminating action of the skin, heat production was in excess of heat-elimination, heat would accumulate in the system . . . the heat-inhibiting centre would be first stimulated to excessive effort, then fatigued and finally paralysed, and hyperpyrexia would result*" (20).[1]

Practically, then, Maclagan views hyperpyrexia in rheumatism as equivalent to the supervention of the phenomenon of *heat-stroke in rheumatism*, with this difference, that in *idiopathic* heat-stroke the condition arises in dealing with heat which is *normally* produced, while "*rheumatic heat-stroke*" (if the phrase be permitted) is due to a failure of the inhibiting mechanism to control the *excessive heat-production* which is a characteristic feature of rheumatism. He consequently defines rheumatic hyperpyrexia as—"Paralysis of inhibition of metabolism, paralysis of heat-inhibition being only part of the process."

I had hoped that some light might be thrown by Dr Hale White's Lectures (17) previously referred to upon this question of the pyrexial process of rheumatism being characterised by excessive heat-formation, but unfortunately I have been unable to discover any reference to experiments or observations upon rheumatism at all.

[1] p. 321.

Criticism of Maclagan's Theory of Rheumatic Hyperpyrexia.

While no doubt objections might be urged to some of the statements upon which this theory is based, a consideration of the various features that characterise the great majority of cases of hyperpyrexia in rheumatism shows that they are certainly not incompatible with such an explanation, and indeed some of the more obscure phenomena are made clearer. It will probably conduce to greater simplicity if, in the light of Maclagan's theory, we examine in order the various characteristics of rheumatic hyperpyrexia as detailed in a previous part of this paper.[1] Thus—

I. The *occurrence of the complication at certain seasons* (often several cases at short intervals with subsequent periods when no case of rheumatism develops it) may arise from a greater difficulty in eliminating the excessive heat at these times. Similarly its greater *tendency to occur in summer*—at a time when cases of rheumatism are not common—might be thus partly explained. It might be urged, no doubt, that hyperpyrexia should ensue much oftener than it does in cases of rheumatism which occur in hot weather, but the element of the *personal factor* in reference to the stability of the nervous organisation always comes in.

II. Further, *the comparative rarity* of this complication is obviously due to the fact that more than one factor is requisite, not only the tendency on the part of the patient to instability of the nerve centres, but, in addition, impaired elimination of heat, &c.

III. As regards *the influence of age* upon hyperpyrexia, we saw that the commonest age for its occurrence is also the period of the greatest frequency of rheumatism. I shall specially refer later on to the bearing of this theory upon the absence of this complication from rheumatism in childhood as previously mentioned.

IV. The *greater incidence of this complication amongst males* has been assigned by several to their greater tendency to alcoholism, with consequent impairment of their nervous organisation. Might it not also be partly accounted for by the fact that in them, owing to the conditions of their daily life, tissue metabolism (and consequently heat-production) is not only much more active, but is also liable to be put to excessive strains? Their heat-controlling mechanism is thus called upon for more constant activity than in the case of females, and might thus be more liable to break down.

V. The *greater frequency of the phenomenon in first attacks of*

[1] p. 6 *sqq.*

rheumatism is obviously due to the presence in the patient of what may be regarded as a *predisposing* cause—the inherent tendency to instability of the heat-regulating apparatus, which is clearly included under Maclagan's phrase "unusual susceptibility of the nerve centres." That such a patient should show a liability to this complication in his *first* attack of rheumatism is only natural, but this subject will be further alluded to when another of its aspects is considered.

VI. *The uselessness of remedies which control the pyrexial* process of rheumatism *for the treatment of hyperpyrexia* in the same disease is also explained. For hyperpyrexia being due, not to the action of the rheumatic poison, but to *paralysis of inhibition of metabolism, anti-rheumatic* remedies are obviously valueless.

VII. The explanation of the *almost universally fatal character of the hyperpyrexia when untreated* (as compared with other instances in which equally high temperatures are recorded) is also self-evident—in the paralysis of one of the most vitally important centres of organization in the body; while

VIII. The very *fact of the success of the proper treatment*, as compared with the results in those cases in which the same mechanism is actually destroyed, such as cases of injury to the cervical spinal cord or the corpus striatum, only emphasises the more that it is a *function* which is abrogated, and not an *organ* which is destroyed.

IX. The *explanation of the efficiency of cold to the surface* of the body *in curing the condition* or *preventing its recurrence* also agrees with the theory propounded; for the action of ice lies in more than a mere abstraction of heat. No doubt this of itself is extremely important; but to admit that this was the *whole* result of its application is, as Maclagan points out, tantamount to regarding the symptoms of the condition as entirely due to the high temperature, which we have just seen is *not* the case. The excessive temperature is merely one of the manifestations of the nervous disturbance, and the chief value of cold applied to the surface lies in its enormously powerful stimulation of inhibition of heat formation. It thus strikes at the fountainhead of the mischief by its action upon the failing nerve centre, while at the same time it facilitates this restoration of the flagging energy by abstracting so much of the excessive heat already formed.

X. The next point is one of the most difficult to explain in the occurrence of hyperpyrexia, viz.—*its tendency to appear in even mild cases of rheumatism.* Were hyperpyrexia the result of an "excessive pyrexial" process, then one would expect it chiefly in *severely pyrexial* cases of rheumatism. This theory, however, regarding, as it does, hyperpyrexia as resulting from essentially

different causes from the ordinary pyrexial process, while it does not altogether explain it, is, at least, not incompatible with such a peculiarity of the complication. No doubt this is not a very strong defence to make of the correctness of Maclagan's hypothesis ; but at least this much can be further said in its support, that the difficulty is not surmounted in any better fashion, as we shall see, by the other theories that might be put forward.

XI. Lastly, *as regards the cessation of sweating*, a characteristic which is, however, by no means universally present, two views might be taken. It might be regarded as evidence of the truth of Maclagan's theory, inasmuch as it suggests the presence of one of the factors he mentions, viz.—" more or less failure in the heat-eliminating action of the skin." But, if looked at more carefully, does this not imply that the real primary cause of the hyperpyrexia is a failure of the *eliminative* mechanism ? Thus it might be suggested that the first step in the process was really (1) *exhaustion* of the *heat-eliminating mechanism* from over-stimulation ; and (2) consequent upon its exhaustion the whole stress of controlling the temperature would fall upon the *heat-inhibiting* centre, which might thus become really *the second link* in the chain of events.

The granting of this other hypothesis does not mean the invalidation of Maclagan's theory ; for the essential feature of this (viz., the excessive heat-formation characteristic of rheumatism) implies equally excessive action of the *eliminative* function in its attempt to prevent undue accumulation. If, then, this excessive stimulation of elimination leads to exhaustion and paralysis of the function, the whole strain will be left to be borne by the *heat-inhibiting* mechanism, which may in turn give way, and not until then will hyperpyrexia ensue.

But even *when there is no paresis of the heat-eliminative* mechanism, hyperpyrexia may ensue. This, I think, is distinctly proved by the occurrence of numerous recorded cases, in which, so far from there being cessation of sweating, this function continues *actively to the end.* Thus it is evidently the failure on the part of the *heat-inhibiting* mechanism which is the *important factor* in the production of hyperpyrexia, the thermolytic mechanism, even when still thoroughly active, being unable to cope with the excessive heat-production in rheumatism unless powerfully reinforced by the activity of the heat-inhibiting function.

While, then, our examination of Maclagan's theory of the pathogenesis of hyperpyrexia in rheumatism brings out that it offers an explanation which is at least quite feasible, it will be necessary to glance briefly at other views which have been put forward.

Other Theories of Rheumatic Hyperpyrexia.

1. It has been suggested by some that the hyperpyrexia is the result of a *direct action of the rheumatic poison* upon the *heat-centres in the central nervous system* (9).[1] This idea is closely related to the old view that "cerebral rheumatism" was a metastasis of the rheumatic process from the joints to the brain, in support of which contention the frequent cessation of joint-pains in hyperpyretic cases was quoted. But this latter is not an essential, for the poison might be supposed to act upon the centres in the brain while still continuing to affect the joints. Apart, however, from the *peculiar rarity* of this *direct* action upon the heat-centres of the poison (which is presumably constantly circulating in the patients' blood in *every* case of rheumatism), and for which infrequency no adequate explanation is given, it must be noted that a similar hyperpyrexia occurs in several other cases in which there is not the slightest ground for believing any rheumatic poison is present at all, *e.g.* heat-stroke, or hæmorrhage into the corpus striatum. Moreover, how should the application of *cold* to the surface of the body *cure* such a condition which, unless thus treated, is practically always fatal? Against the suggestion which might be offered that it was only in cases of *virulent* poison that this affection of the nerve-centres occurred is the well-known fact of the frequent occurrence of hyperpyrexia in cases of rheumatism with *mild* symptoms, which would not likely be the case were the rheumatic poison of a specially *virulent* type.

2. Perhaps, however, the suggestion might be urged that—still adhering to the view that the hyperpyrexia is the result of some *poison* upon the heat-centres—the materies morbi might be something *distinct from* the rheumatic poison—possibly some (*a*) *other poison* present *along with* that of rheumatism—as in what is called, in surgical pathology, cases of "mixed infection"; or (*b*) a *product of its action*—a toxine, so to speak. (*a*) The fact of the pyrexial process having shown in at least several of the cases little sign of being controlled by the salicyl compounds might, no doubt, be adduced in support of the view that some other fever-producing substance is present on which the specific anti-rheumatic drug has no effect; but on the other hand so many of the cases which develop hyperpyrexia have presented clinical features differing in no respect from ordinary *simple* cases of rheumatism, that the former of these suggestions is very improbable; for one would expect a case of "mixed infection" to show, if not *unusual*, at least *severe* symptoms; while the remark made upon the success of treatment by cold under the previous hypothesis holds equally true in this connection.

[1] p. 266.

(*b*) In favour of the "toxine" theory, perhaps rather more evidence might be adduced. While the phenomenon under consideration is quite different from the nervous (paralytic) disturbances frequently seen in cases of diphtheria (now generally admitted to be the action of toxines), are there not some grounds for regarding rheumatic hyperpyrexia as in some respects allied to that "complex of symptoms" (as it is called) known as *diabetic coma*? No doubt the exact pathology of this latter phenomenon is as yet unknown. The clinical picture, however, in the two cases presents rather a striking resemblance, not merely in the mode of onset, with its prodromal symptoms of cerebral impairment or excitement, with restlessness, insomnia, and (in diabetic coma) markedly altered type of respiration, passing into coma in both instances, but also in the fact of the frequency of the supervention of the complication in cases which have previously shown no symptoms of unusual severity, the one striking contrast being the absence of excessive temperature in a diabetic comatose case as compared with the patient in a state of "rheumatic coma," if I may use the expression. In the *former* the *respiratory* mechanism is the one which appears to be most perturbed by the poison, while in the *latter* the disturbance is chiefly manifested apparently in the *heat-regulating mechanism*. Is it possible that the poison might be some product of perverted tissue-metabolism arising in certain cases, and setting up, by its toxic action upon the central nervous system, the various nervous phenomena, *e.g.* insomnia, delirium, and coma, with occasional convulsions, as well as the disorganisation of the heat-regulating mechanism, the nature and exact localisation of which is not known? Such a theory is, of course, purely speculative, but it might be possible to bring the hypothesis in several respects into accord with the facts known regarding the phenomena presented in rheumatic hyperpyrexia. Thus the comparative *rarity* of the complication might be explained, as being due to the necessity for the coincident occurrence of the two factors which might be requisite for its production—a special variety of rheumatic poison or some peculiarity of the metabolic processes special to the individual; and similarly the *suddenness of its supervention* in apparently typical cases of acute rheumatism is quite on a par with the clinical characteristics of diabetic coma; while the method of treatment successfully adopted in a case of rheumatic hyperpyrexia by H. Barré (2),[1] by the process which he terms "Disintoxication of the Blood" (as alluded to subsequently under the heading of treatment), is curiously suggestive of the treatment advocated for cases of diabetic coma by means of transfusion of saline solution.

Before venturing even to suggest that the explanation of the

[1] p. 230.

phenomena of rheumatic hyperpyrexia might be found in such a theory, a much more elaborate examination and comparison of the features of the two conditions—viz., diabetic coma and rheumatic hyperpyrexia with coma—would be required, but enough has been said to indicate that this line of investigation might throw some light upon the pathogenesis possibly of both conditions.

3. The only other aspect of the pathogenesis of hyperpyrexia in rheumatism which it is necessary to allude to is the view which was formerly held that the occurrence of the condition is due to the *presence of visceral complications*, and especially *pericarditis*. That such complications frequently *are* present is undoubted, and that their supervention upon an ordinary attack of acute rheumatism will often lead to an *exacerbation of the pyrexia* in that attack is equally true, but these facts do not at all account for the marked *nervous* phenomena which are equally characteristic of rheumatic hyperpyrexia, nor yet its practically universally *fatal* character. For pericarditis and such complications occur not infrequently in other diseases, *e.g.*, Bright's disease, *without* any such hyperpyretic manifestations, or accompanying nervous phenomena. Moreover (and this is a point which, though very striking, has not received sufficient notice, so far as I can discover), we shall see that it is *especially* in the rheumatism of *childhood* that the *visceral* manifestations of the rheumatic poison occur most frequently, while it is just *in those very cases* that hyperpyrexia is *not* found. But over and above those various reasons, the undoubted fact of the absence of any such complications, as has been proved now by ample data from necropsies in fatal hyperpyretic cases, definitely settles the question as to the possibility of this being the true explanation.

As a result, then, of our examination of the various theories which have been put forward to account for the clinical phenomena comprised under the term "rheumatic hyperpyrexia," the balance of probability appears to lie with that of Maclagan, which not only affords a feasible explanation of the pathogenesis but is also quite in consonance with the various characteristic features of the condition.

Before leaving this part of our subject there are two other points which appear to me worthy of special notice in reference to this theory of Maclagan's as to rheumatic hyperpyrexia. The first has reference to the

Recurrence of Hyperpyrexia.

Should it not be expected that patients who have once shown this phenomenon in an attack of rheumatism would again be liable to a recurrence of the condition if they have

subsequently another attack of the same disease? I have already intentionally quoted Maclagan's words in reference to what one might term the predisposing cause of the condition, where he speaks (20) [1] of "an unusual susceptibility of the nerve centres" as probably having some part in its production. If then a patient has this tendency to instability of his heat-regulating mechanism one would expect not only the complication to arise in his first attack (this we have seen to be the rule) but also that subsequent attacks of rheumatism should have a tendency to reproduce the same complication and all the more since the previous paresis of the mechanism might be expected to have left it in a weaker condition than formerly. There are probably few diseases in which the tendency to subsequent attacks of the malady is more widely recognised, and the fact of the recurrence of such a complication as hyperpyrexia would surely be noted by those who have published instances of the condition. But, as before mentioned, not a single instance of the reappearance of hyperpyrexia in the same patient during a subsequent attack of rheumatism can be found amongst the *published* cases which I have been able to collect, ninety-four in all, my own solitary case of A. S. being already noticed previously (page 15). It is difficult to explain this absence of any published reports of such a recurrence of rheumatic hyperpyrexia. It is just possible that, with the previous history in view, subsequent attacks of rheumatism in such individuals are so watched that the *prophylactic* treatment of hyperpyrexia comes in to explain the apparent anomaly, but one would have expected that surely a few instances would have occurred and been deemed worthy of recording. While, then, unable to account for this rather strange statistical anomaly I thought it at least worthy of a passing notice.

The other point I wish to draw attention to has reference to

Rheumatism as it occurs in Children.

I have already mentioned that Maclagan in his arguments in support of the miasmatic theory regards rheumatism as rare in children, and he goes on to show (20) [2] that the possible explanation of this rarity lies in the fact that "the action of the rheumatic poison is almost confined to . . . those parts of the fibrous and serous tissues of the body which enjoy a high degree of functional activity." He then suggests that in childhood the joints and especially the muscles have not reached this period of greatest functional activity and that therefore rheumatism does not occur in childhood. But, as before alluded to, abundant evidence exists to show that rheumatism does affect children very markedly,

[1] p. 320. [2] p. 233.

although the phenomena they exhibit during its course are not modelled on the type of rheumatic fever in adults, in whom the arthritic symptoms and profuse sweatings are usually the most prominent features. In children, on the other hand, as is so frequently pointed out, especially by Cheadle, "arthritis is at its minimum while pericarditis and endocarditis," etc.—other manifestations of the action of the rheumatic poison—"are at their maximum" (4)[1]; and again, "in early life, the fibrous tissues of the subcutaneous fasciæ, tendons, pericardium and endocardium are far more sensitive to the morbid stimulus . . . than the same tissues in later life."[2] It is because of this difference in its clinical features at different ages that Cheadle puts forward the plea for regarding the disease as it occurs in *children* as the true type of acute rheumatism, because in them manifestations of the action of the rheumatic poison are seen which do not present themselves after adolescence.

While then the *occurrence of rheumatism in children* is undoubted—(Fagge mentions (13)[3] that even in a general hospital like Guy's out of 365 cases of "first attacks" of rheumatism no less than 6% occurred in patients between the ages of five and ten), — the *almost entire absence of rheumatic hyperpyrexia* amongst them is just as well proved as we have already noted.

Explanation of the Absence of Rheumatic Hyperpyrexia in Children.

Now, are there any special characteristics in the rheumatic process in childhood, which might serve to give an explanation of this absence of hyperpyrexia? Of all persons, surely in *children*, in whom often the very slightest causes will induce a marked degree of pyrexia, one would expect this feature of "excessive" temperature to present itself. Undoubtedly so, if the hyperpyrexia of rheumatism is really "*excessive*" pyrexia. We have, however, held it as proved in a former portion of this paper that it is *not so* at all, but the result of quite a different process. In the light, then, of Maclagan's suggestion as to the influence of functional activity upon the localisation of the rheumatic process, might one proffer the suggestion that *hyperpyrexia is absent* from *rheumatism in children*, because in *them there is awanting* the *excessive heat-production of rheumatism in adults?* There would seem to be sufficient grounds for such an explanation in view of the following facts:—

1. *Arthritis* is comparatively a *very slight phenomenon* in rheumatism in children. Cheadle says (4)[4]—"The articular affection . . . is usually slight and subordinate, and, indeed, may be

[1] p. 8. [2] *Op. cit.*, p. 107. [3] Vol. ii. p. 694. [4] p. 8.

absent altogether from a seizure undoubtedly rheumatic in its nature."

2. The *same is true of sweating*; practically never is the excessive and acid sweating of the adult type of rheumatism to be met with. The same authority says[1] again—"The profuse sweating, one of the typical symptoms in the acute rheumatism of adults, is rarely seen in children, the rarity being in inverse proportion to age. It only begins to appear with more severe joint affection as age advances."

Now if the rheumatic poison in children affects the fibrous tissue of the peri- and endocardium and the subcutaneous fasciæ rather than the joints and muscles, because in the *former* is situated the nidus requisite for its propagation, then there will be less *sweating*. For, according to Maclagan (20),[2] lactic acid, which acts as such a powerful stimulant to the sweat glands, is not a product of metabolism of white fibrous tissue structures (consisting as they do chiefly of nitrogenous tissue) to anything like the same extent as is the case with muscle (non-nitrogenous). The difference in the *clinical* type of the disease in the two cases is thus explained.

But further, the metabolic process which goes on in the case of these fibrous and serous structures is a much less active one, so far as concerns the production of *heat*, than that of the metabolism of muscles, and much less heat is consequently produced. Thus Cheadle says (4),[3] when speaking of the mild pyrexia of rheumatism in childhood as compared with adults: "it must be chiefly the arthritis which raises the temperature."

Chemically, then, so to speak, the rheumatic process in children is characterised by much *less heat-formation*, and hence there is no call whatever for extra stimulation of the inhibitory function, just as there is nothing to produce fatigue of the eliminating mechanism. Paresis of the thermotaxic mechanism, therefore, from over-stimulation is practically impossible. Briefly stated, then, the suggestion I would offer to account for the absence of hyperpyrexia in the rheumatism of children is this:—Since the rheumatic poison *during childhood* finds its nidus chiefly in the *fibrous tissues*, there is *less heat produced* (the chief seat of heat-formation being muscle); consequently there being no excess of heat-formation, *no strain is put upon* the *heat-regulating mechanism*, and therefore *paresis of this* mechanism *from over-action could not be looked for*.

That the nidus suitable to the rheumatic poison should be situated in different tissues at different ages is quite in consonance, I think, with what we know of other pathological processes. Thus is there not a parallel instance in the recognised incidence of *tubercle* upon the *cerebral meninges* rather than the

[1] *Op. cit.*, p. 32. [2] p. 236. [3] p. 33.

pulmonary tissues in *children*, as compared with *adults*, in whom the relative frequency of incidence is just the opposite?

It might be said, however, that a *mildly pyrexial* case of rheumatism in an *adult* is on a par with the *type of rheumatism* in *childhood* since the production of heat in such a case is evidently not very extreme, and yet hyperpyrexia frequently occurs, as we know, in mild cases of rheumatism in adults. No doubt this is true, but while the mild case of adult rheumatism *appears* to be essentially similar to the type present in children it is *not really* so, for in the former the pathological process of the disease is going on in a different set of tissues, viz., the *muscular*, as witness the lactic acid sweats.

Clinical Evidence upon this Theory.

I thought it might be of interest to see whether the rare cases which have been recorded of rheumatic hyperpyrexia at an early age presented the features of rheumatism of the *adult* type, *i.e.* with joint-pains and sweatings, rather than the form characteristic of *childhood* with these phenomena in comparative abeyance. I can find *only four* cases mentioned in which hyperpyrexia ensued in patients with acute rheumatism under the age of fourteen, two described by Barlow (1),[1] a boy aged ten and a girl of thirteen respectively, one mentioned by Donkin (10)[2] at the age of twelve, a boy, and a fourth in the Clinical Society's collection (7),[3] that of a girl aged thirteen; and it is rather remarkable and significant that the notes of these cases record respectively the facts of (1) "pains in large joints"; (2) "severe rheumatism affecting many joints"; (3) "patient lying bathed in sour-smelling sweat and screamed with evident pain on movement of his limbs"; (4) and lastly during the hyperpyrexia "joint-pains diminished" and the skin subsequently showed "return of sweating." By the great kindness of Professor Fraser I was enabled to see the notes of another—a *fifth* case of hyperpyrexia in a patient aged twelve, a girl whom he had under his care in the Royal Infirmary in October 1896. In a subsequent portion of this paper I shall avail myself of his kind permission to allude to the chief features of the case in illustration of another point; here I wish merely to note that the record of the clinical history brings out the very same facts as to the rheumatism in her case also having been of the *adult* type. She is described as having on admission "characteristic rheumatic sour-smelling sweating," while the "knees, ankles and wrists are painful and the ankles are swollen."

So far, then, as one is justified in drawing conclusions from such a small number of cases, the evidence thus adduced

[1] p. 512. [2] p. 212. [3] p. 312.

would appear to support the theory of Maclagan, and suggests the further proposition (1) *that hyperpyrexia in rheumatism is a phenomenon whose occurrence depends rather upon the* TYPE *the rheumatic process assumes than upon the exact* AGE of *the sufferer;* and (2) that *instead* OF VISCERAL "*complications*" *or manifestations of rheumatism being causally associated* as some have supposed *with the occurrence of hyperpyrexia, it would appear that the* ARTHRITIC *phenomena are probably the essential features for its production.*

While fully conscious of the relatively minor importance of these conclusions I ventured to regard them as not altogether without interest, and all the more worthy of recording in view of the very great dearth of any reference in the literature of the subject to this problem of the *explanation* of this *absence of hyperpyrexia in rheumatism in children.*

Mortality: Prognosis.

That hyperpyrexia in rheumatism has an exceedingly grave significance is a point which has been more than once alluded to. The *average mortality* of *acute rheumatism* is probably about 3%; the Collective Investigation Report (8) [1] gives it as 3·3%, and the Clinical Society's Report (7) [2] as 2·6%, calculated from 1300 cases; while I notice in the recent volume of the Edinburgh Hospital Reports (12) [3] that the total cases of acute and subacute rheumatism treated in the Royal Infirmary during the five years 1891-96, amounting to 837, contains twenty fatal instances, giving an average mortality of 2·3%.

The importance of hyperpyrexia as an element contributing to this mortality, is vividly brought out when Fagge's statement (13) [4] that "at least 14 patients died of hyperpyrexia in acute rheumatism in Guy's Hospital between 1870 and 1877," is compared with the figures he gives on the same page showing the total mortality of rheumatic cases between these years to have been 38. Thus of these 38 deaths from rheumatism nearly 37% were due to hyperpyrexia alone. This undoubtedly overstates the mortality from hyperpyrexia in rheumatism, for we have already seen that the period Fagge deals with includes those very years during which hyperpyrexia was shown by the Clinical Society's Report (7) [5] to be unusually prevalent. But the much smaller percentage given by Bryant (3),[6] that of the fatal cases collected by him, 17% owned hyperpyrexia as the cause of death, is still sufficiently convincing proof of the importance of this complication in producing the death-roll of acute rheumatism.

[1] p. 401. [2] p. 268. [3] Vol. v. p. 299.
[4] Vol. ii., p. 697. [5] p. 263. [6] p. 402.

It is not surprising, therefore, when we come to consider the mortality of the hyperpyretic cases themselves, to find that this is very high. In the Clinical Society's Report, based on 67 cases, it is given as 49·2%, while Bryant, dealing with 83 cases, gives it as even higher, viz., 56·7%, but it must always be borne in mind that he includes only cases with temperature "above 106°," while out of the list of 34 *recoveries* in the Clinical Society's Report (7),[1] no fewer than 20 showed a temperature record *not exceeding* 106°, the deaths for the same temperature limits numbering only 8. That the mortality of cases of hyperpyrexia is greatly influenced (1) by *the height to which the temperature rises* is clearly brought out, though this latter is rather the indication of the severity of the case than the cause of it. Thus while in the Clinical Society's cases, none of the patients with a temperature over 110° recovered, and of cases between 108·1° and 110° only 2 recovered and 13 died, there were 8 recoveries to 3 deaths in the cases with temperatures between 106·1° and 107°. That such should be the case is only to be expected, for a case with such a high temperature as 109° or 110°, almost certainly implies that the disturbance of the cerebral functions has been of longer standing, and has thus caused more serious damage before treatment is applied, than in cases where the temperature is kept from rising beyond more moderate limits.

This suggests the second important factor (2) in influencing the mortality, viz., *the treatment employed for the cure of the hyperpyretic condition.*

Prior to the adoption of the various methods of application of cold for this object, the cases were almost uniformly fatal. After Wilson Fox (14), however, clearly demonstrated not only the existence of the hyperpyrexia, but the undoubted benefits of cold in its treatment, cases of recovery after even high temperatures began to be recorded. It was not till several years later, however, that the facts became generally recognised, that not merely was the application of cold a successful method of treatment, but that practically it was the *only* satisfactory method, and that treatment by drugs only meant the loss of valuable time during which the temperature might rise still higher with greater danger to the patient. And not only so, but the wider acceptance of such views has resulted in the employment of such measures as a *prevention* of the condition, so that at the onset of the prodromal symptoms, cold is employed in the treatment of the patient before the temperature has attained extreme limits. This adoption of prophylactic treatment *should* result in not merely a reduction in the *frequency* of the complication (a point already referred to), but also

[1] p. 298.

in a *lowering of the percentage mortality* of the hyperpyretic cases.

I thought it might be interesting to see if an examination of the various collected cases brought this out, and I have gone over the records for this purpose, taking as the dividing date between the early and later methods of treatment the year 1882, this being the year of the publication of the Clinical Society's Report on hyperpyrexia in acute rheumatism, which first brought the subject prominently before the profession. This date has the further advantage of dividing equally the thirty years from Ringer's first published case down to the present year into two periods of fifteen years.

The 96 cases taken for this purpose consist, as previously mentioned, of Bryant's collection of 83—all of which, it should be remembered, had a *temperature of* 106° *or more*—with 8 more published cases (collected from various journals) subsequent to the date of his article, as well as the 5 unpublished cases described in this paper by myself. The analysis of these cases brings out the result shown in the annexed table :—

CASES OF HYPERPYREXIA IN RHEUMATISM.

	1869-1882.	1883-1897.
Total cases . . .	49	37
Fatal	28	20
Percentage mortality .	57%	54%

[Ten cases in which the date of the hyperpyretic attack is not given are excluded.]

This rather surprising result, then, is brought out that the mortality, as calculated from the recorded cases to which I have got access, is practically the same in the two periods chosen for comparison. Now does this really mean that the mortality of this condition is *as great nowadays as formerly?* Such a conclusion, I think, would be erroneous, and for the following reason. Cases of the condition are not now so frequently recorded as formerly, the treatment by application of cold having become so recognised as the essential thing that cases of recovery from rheumatic hyperpyrexia are no longer published as noteworthy. A similar state of matters is more or less noticeable in connection with the introduction of any new remedy, *e.g.* diphtherial antitoxin of which the cases which are now recorded (as compared with the time when the treatment was first introduced) are the *failures* rather than the successes in its application. So in regard to hyperpyrexia,—it is the *unsuccessful*, rather than the successful, instances which are now published. It is from the *continuous records* of hospital cases that one would perhaps get the truest estimate of the actual mortality of the condition,

though even these are apt to be vitiated, as we have seen, owing to severe cases being sent there for treatment often in practically a moribund condition. Moreover, it is evident from an examination of the records of the cases that the employment of cold in the treatment of this grave complication is still *by no means universal*, so that one cannot draw really any distinction between the older and more recent results in this manner, for in several instances various antipyretic drugs are still relied upon to remedy the condition.

While, then, a consideration of the statistics above referred to does not bring out any material reduction in the mortality amongst hyperpyretic cases, there is little doubt that the prognosis —when various considerations are taken into account—is *better* amongst those which are treated by *cold* applications than by other methods. This is brought out in the Clinical Society's Report, which points out (7) [1] that while the mortality is practically the same in both groups if the "*bathed*" cases are compared with the "*non-bathed*," yet, when along with the question of treatment is combined that of the *degree of hyperpyrexia present* the advantage in the *former* group is clearly brought out. Thus—

	Total.	Died.
Of the "non-bathed" cases with temperature above 106°	5	5
„ "Bathed" „ „ „ „ „	34	20

giving a mortality of 59% in the "*bathed*" cases as compared with 100% in the case of the "*non-bathed*."

So far as concerns the influence of *age* upon the mortality of hyperpyretic cases but little evidence can be deduced, an examination of the 96 cases showing that fatal cases appear as frequently amongst young adults as amongst those in later years, due allowance being made for the greater preponderance of rheumatism, and especially "first attacks," in adolescent life.

The importance attached by the Clinical Society's committee in their report to the prognostic significance of *early onset of the delirium*, as indication of an especially *grave* type of the complication, has already been referred to.

One other matter in regard to the immediate prognosis is this—Is there not a possibility of a patient who has been cured of his hyperpyrexia dying in consequence of some after-result of the treatment employed? Thus, in the case I related at the beginning of this article,[2] there was abundant evidence that, subsequent to the employment of cold for the initial hyperpyrexia, acute nephritis developed (as shown by the blood and casts present in the urine). Now, is it not possible, if indeed it be not probable, that this was largely the result of the chilling of the surface of the body, especially in the case of a patient the ex-

[1] p. 286. [2] p. 6.

cretory functions of whose skin were manifestly out of order? No doubt the comparatively innocuous results of the employment of cold baths, &c. in the treatment of other diseases, such as enteric fever, might be adduced as evidence against such a suggestion; but there is this important difference, that in these latter cases there is no failure of the eliminative functions of the skin as is so frequently the case in patients with rheumatic hyperpyrexia. Of the extreme gravity of such a complication as acute nephritis (however induced) in a hyperpyretic case there can be little doubt, for treatment of acute Bright's disease in a patient whose sweating apparatus is out of order holds out but little prospect of success. We must therefore never lose sight of the fact that, having rescued our patient from the primary danger of the hyperpyrexia, his ultimate recovery may be greatly hampered, if not rendered altogether impossible, by reason of such grave consequences of the necessarily severe treatment adopted.

As regards the *ultimate* prognosis in hyperpyretic cases, in addition to the risk of these sequelæ becoming permanent, it is, I think, possible that more or less serious damage to the cerebral functions may result apparently from the high temperature. Certainly one of my cases (A.S.) showed for a considerable time that condition described by our Scotch phrase, a decided "want."

TREATMENT OF HYPERPYREXIA IN RHEUMATISM

PASSING on now to the treatment of this evidently very grave complication, we happily find ourselves upon much more certain ground. However much difference of opinion may prevail as to the *etiology* and *pathogenesis* of hyperpyrexia in rheumatism, all observers and investigators of the condition are at one in regard to its *treatment.* The question of treatment has to be considered under its two aspects—(1) as regards the *prophylaxis* of the condition and (2) the *remedies* for the complication when present, but it will be simpler if the latter of these is taken first.

The earliest record of the employment of the now almost universally adopted method, consisting in the application of cold in one of its forms, appears to be a case described by Meding in 1870 in the *Archiv. f. Heilkunde*; but in this country at least the name of Dr Wilson Fox will always be remembered as having been the first to draw the attention of the medical profession to the subject by the publication of his articles in the *Lancet* in 1870, and subsequently in book form, on the treatment of hyperpyrexia (14). In the latter he gives full details of three cases, two which occurred in 1871, both successfully treated, the third, an unsuccessful one, at an earlier date—1869. So carefully were these cases watched and treated, and so thorough are the records given of them, that an examination of them reveals the fact that but little further progress has been made in regard to the details of this method of treatment since the publication of what may be regarded now as a classical contribution to medical literature.

The methods which have been adopted in different cases vary considerably, but essentially they all have the same aim in view—rapid abstraction of heat from the body. Perhaps the most widely advocated and best method is by the use of *the cold bath* — the temperature of the water being graduated as required. The patient, who, as we have seen, is usually comatose or almost so, is lowered on a sheet into a bath containing water at a temperature about 90°, the water being then quickly reduced in temperature to about 70° or even lower. This is preferably accomplished by means of ice, which may at the same time be rubbed over the patient's body. His temperature must be continuously taken, usually in the rectum, by a rapidly recording thermometer, the one essential point to ensure success in the treatment being this, that he must be removed from the

bath before his temperature has reached normal,—indeed it is not safe to continue the cold bath after the patient's temperature has fallen to 102° or thereby. The reason of this lies in the fact that the temperature continues to fall for some little time after the patient is removed from the direct influence of the cold surrounding medium, and hence, should his removal be delayed until his temperature has been brought down to its *normal* level, the subsequent continuous fall after his removal from the bath results in dangerous collapse with persistently *subnormal* temperature. This unfortunate result was well-marked in the case of A. S. during the treatment of his *second* attack of hyperpyrexia in 1894, as recorded previously,[1] where we saw that for nearly two hours after his removal from the cold bath his temperature continued at 95°, with a pulse-rate of 44, and the patient showed such signs of collapse that hot bottles to the surface of the body with vigorous friction, brandy by the mouth and subcutaneous injections of stimulants were all required for some considerable time to enable him to survive the results of the too vigorous application of cold for the cure of the initial hyperpyrexia. So soon, then, as the patient's temperature falls to 102°, he should be removed, dried, and placed on a dry bed with only a light coverlet, his temperature being still taken regularly at a few minutes' interval so as to guard against either a fall to subnormal or a return to excessive limits as before.

The time the patient requires to remain in the bath varies considerably, chiefly with the initial temperature of the water and the extent to and rapidity with which this is reduced, but the main point to be attended to is the condition of the *patient's temperature*, and the question of the time for his removal is settled by this as well as his general condition, rather than by any arbitrary data as to the duration of the cold bathing. It is apparently not advisable to have the temperature of the water too low on his first immersion, but the subsequent cooling of the water is usually rather grateful to the patient than otherwise.

Now it is quite obvious that this method of treatment by immersion in a bath implies a condition of matters frequently unobtainable, viz., several (more or less trained) assistants and a conveniently situated or portable bath—conveniences as a rule to be had only in a well-equipped hospital. But, as a result of a wider diffusion of the good results obtainable from the employment of cold in this condition, ample evidence has been now collected to prove that other methods than that of cold bathing are equally efficacious.

One of those most frequently employed is the *general ice-pack* to the whole body, the patient (covered merely with a thin sheet and lying upon waterproof sheeting) being packed round with

[1] p. 16.

pieces of ice, some of which are rubbed over the head and chest, while the lower surface of his body lies in a pool of almost ice-cold water. [In the case of A. P. first recorded here, this method was employed in his initial attack after the cold bathing had been done, but the method of treatment by the ice-pack was so much more easily carried out, that when vigorous treatment was again required in his case this method was always subsequently resorted to rather than the bathing. The difficulty of keeping a comatose patient in a bath of water, the quantity of which is being changed by addition of colder water, without letting the mouth get under the surface is sometimes very great, especially when, as in this instance, the patient is a tall and very heavy man.] Here again, as in all the methods employed, the same precaution as to guarding against excessive reduction of temperature is essential, the patient being lifted on to a dry bed as soon as a fall of his internal temperature to 102° is recorded.

Should no ice be available, as may be the case in country practice and especially in summer—the most frequent season, as we have seen, for the condition arising—ordinary cold water may be used, sheets or towels wrung out of this being continuously applied to the patient, the surface of whose body may at the same time be fanned to aid the evaporation of the damp sheets and so produce a further abstraction of heat. It has even been suggested that a fairly satisfactory substitute for a cold bath may be obtained in almost any house by having one end of the bed raised while the lower end is directed over a tub, and the patient vigorously "sluiced" down with pailfuls of cold water, which runs off into the tub at the foot.

When the temperature, as in some cases, is not so excessive, less vigorous methods of application of cold may be sufficient, such as large ice-bags to the abdomen and chest, or the ordinary cold pack by means of a sheet wrung out of cold water; in milder cases even tepid or cold sponging of the surface of the body may suffice. Such methods of treatment are adapted more for cases when in the earlier stages of hyperpyrexia, and their chief rôle perhaps comes under the subject of the *prophylaxis* of the condition.

By one or more, then, of the above methods of application of cold to the surface of the body is the condition of hyperpyrexia in acute rheumatism now almost universally treated, and in regard to all of them the following facts are to be noted as having been practically proved:—

1. *That the presence of visceral complications in the patient is no contra-indication to the employment of cold in hyperpyrexia.* Numerous cases have been recorded where evidence of severe visceral complications was present in patients who developed hyperpyrexia and who nevertheless underwent the severest forms

of treatment by cold with perfect success. Thus one of the very earliest recorded instances—Wilson Fox's second case—had (14)[1] "double pleuropneumonia and pericardial effusion," and yet not only was the hyperpyrexia successfully combated by cold baths but complete recovery from the various complications ultimately ensued; while a similar instance is reported by Dr Monro quite recently,[2] the patient in this case also making a complete recovery in spite of double pneumonia, although bathing had to be continued for nearly a fortnight.

I have already alluded to the possibility of some risk being run of congestion of internal organs ensuing as a result of the chilling of the surface, but the fear of this must not deter us from employing what is admitted to be the only remedy for an otherwise certainly fatal condition.

2. *The remedy should be tried even in cases which, from the patient's general condition, appear absolutely hopeless.* To illustrate this I need only quote Dr Fox's description of his first successful case, who had a temperature of 110° when the treatment was applied. He says (14)[3]: "She was absolutely unconscious, the pulse was imperceptible, the face highly cyanotic, and she was drawing the few last irregular, gasping, stertorous respirations which commonly precede the act of death," and yet this patient left hospital perfectly recovered by the thirtieth day thereafter. After such a record one need never despair of saving even the most desperate-looking case, and many similar records could easily be adduced emphasising the necessity for trying to rescue even the most hopeless cases. No doubt instances of patients having died while in the bath have been published (and possibly still more remained unpublished), but the absolute certainty of a rapidly fatal termination to the condition when untreated is our warrant for employing what may appear to the relatives a drastic remedy.

The importance of the administration of *stimulants* not only by the mouth and per rectum but also hypodermically if need be, is insisted on by many observers, and in some cases very large amounts have been administered—nearly 30 ounces of brandy alone, besides eggs and milk, were given by Fox in the course of twenty-four hours to one of his cases. It is advisable to give some alcoholic stimulant not merely before the treatment by cold is begun but during the bathing as well, and often, as in the cases of A. P. and A. S., for some considerable time after. It is worthy of note, however, that the earliest recorded successful case—that of Meding—appears to have had no stimulants administered, according to Dr Fox. Obviously the question of the necessity for their administration is to be decided by the *general condition* of the patient apart altogether from his *temperature record.*

[1] p. 37. [2] *Glasgow Med. Journ.*, April 1898, p. 283. [3] p. 4.

But unfortunately the reduction of the initial hyperpyrexia by the cold bath is frequently insufficient to put an end to this dangerous complication. In many cases the excessive temperature tends to recur again and again, so that the bath may have to be employed repeatedly ere the case terminates, two patients mentioned in the Clinical Society's Report having been bathed no less than twenty-six times before their temperature resumed the usual normal limits. Similarly cases which have been treated by an ice-pack or wet-pack may require such remedies to be employed more than once, while in other instances—*e.g.*, the case of A. S. during his second attack of hyperpyrexia—a milder form of the application of cold, such as sponging or an abdominal ice-bag, may be sufficient—once the excessive temperature has been reduced—to maintain it within ordinary pyretic limits. A method which would appear to hold out prospects of success in the treatment of these cases of recurrent hyperpyrexia is the employment of the *continuous ice-coil*, by the use of which the pyrexia may be kept within moderate limits more persistently than is possible when *intermittent* cold applications are relied upon.

Many of the ordinary antipyretic drugs have also been employed with the same object as in the case of A. P., to whom at various times salicylate of soda, antipyrin, and antifebrin were administered to prevent the temperature passing to hyperpyretic limits, but too often, as in his case, with but little effect. The use of such drugs, however, *to prevent the temperature rising again* to extreme heights must be distinctly differentiated from the use of the same remedies to *cure hyperpyrexia when present*—a question to be alluded to presently.

I have yet to mention what is perhaps the most interesting result of the treatment of hyperpyretic patients by means of cold, viz., the marvellous *improvement in the general condition of the patient* which so frequently occurs. Nothing is more striking than to see the patient, who when first placed in the bath was perhaps wildly delirious, or, more probably, absolutely comatose, with stertorous breathing and imperceptible pulse (the condition of my first case, A. P.), become in a few minutes conscious and able to speak intelligently, the respiration returning to its natural condition, while the pulse improves in strength as it falls in rate. It is probably one of the most instructive lessons in the prompt and judicious employment of the appropriate remedy that medical therapeutics can show. No doubt such a remarkable result apparently goes to prove the view held by some, that the hyperpyrexia is the cause of the whole condition rather than, as we are inclined to believe, merely one of its manifestations, but the well-known fact previously mentioned, that temperatures as high, and even higher, occur under many other conditions

without such coincident nervous phenomena, must never be forgotten.

Antipyretic Drugs as Remedies for Hyperpyrexia.

Reference has more than once been made to the uselessness of the ordinary pharmaceutical preparations employed for the control of *pyrexia* in preventing or restraining the *hyperpyrexia* of rheumatism. In the earlier years when its treatment by ice and cold baths was introduced by Meding and Fox, there was no such armamentarium of antipyretic drugs as is now at our command, but in spite of the multiplication of such remedies none has been found to have any material power in controlling hyperpyrexia. I need only allude to one of the most recent illustrations of this powerlessness of such remedies in the treatment of the condition. The case, which is reported by Dr Sloman,[1] was that of a female, aged forty-one, who was treated for "rheumatic pains in the joints" with "salicylate of sodium every four hours, and Dover's powder night and morning." The temperature kept "about 102° for four days, when it suddenly rose to 105°." Antipyrin was then given "in frequent doses," but the temperature, "after ranging between 104·2° and 105° for twenty-four hours, rapidly rose to 110·5°" and death ensued.

The *pyrexia* of acute rheumatism may be said to be under our control, by means of the salicyl compounds, to a degree that has scarcely any parallel amongst other diseases, and the extraordinary change in the temperature records of cases of acute rheumatism, which has been brought about by the wellnigh universal adoption of these remedies, is one of the most notable triumphs in recent practical therapeutics. But, as we have seen, not only does hyperpyrexia ensue in cases which are under this method of treatment—and indeed apparently improving under its employment—but the various salicyl preparations, even in large doses, have been repeatedly proved to be absolutely valueless in checking the condition. The reason assigned for this lies in the fact, as we have seen, that hyperpyrexia is believed to be due not to an excessive degree of the ordinary pyrexial process of acute rheumatism but to a loss of control of metabolism. *Anti-rheumatic* drugs, therefore, could not be expected to be of any service. But what of those remedies which are "antipyretic" by other methods? Without entering into the theories held as to the means by which these various preparations bring about their results, it is only necessary to state the fact, which has been shown over and over again by published records, that each in turn is practically powerless in dealing with the "excessive" temperature in this condition. Perhaps it is only right that

[1] *Brit. Med. Journ.*, 1898, i. p. 817.

I should refer to a case which I find reported by Dr Godfrey,[1] which apparently contradicts this statement. Briefly summarised, it is that of a female, aged thirty-three, who was seized with an ordinary attack of acute rheumatism on October 1st, perspiration being "profuse." On the 4th the temperature, which had been previously about 102°, ran up to 106·5° and "perspiration stopped," while again on the 5th it rose to 106°, and "on both occasions antipyrin gr. x quickly reduced the temperature." Next evening, however, the temperature, which had been 100·6° at 9.30 P.M., was found five hours later to be 112°, the patient being comatose and dying half an hour later in spite of cold packs. Despite such a record, however (which appears to show that antipyretic remedies were of avail at the outset), there can be little doubt that, in the meanwhile, this fact appears certain, that attempts to combat the condition by such means are not only *fruitless* but *dangerous*, for it has been clearly proved that the higher the temperature before the treatment by cold is commenced in any case so much the less is the prospect of success.

In regard, however, to the employment of such antipyretic drugs, there is another aspect of the question; are they of any service in *preventing the recurrence of* hyperpyrexia once the temperature has been brought within ordinary limits by the use of cold applications? To this I think the answer can not be so unhesitatingly negative. No doubt in the first case described, A.P., the various drugs successively administered—antipyrin, antifebrin, sodium salicylate—appeared to exercise no control whatever on the rising temperature, which had always to be reduced by means of cold, but in milder cases, at all events, published records seem to indicate that such drugs as quinine regularly administered have some influence in preventing excessive rises of temperature, though it is difficult to prove this, other means, *e.g.* the use of an ice-cap to the head or abdomen, being frequently combined with the administration of drugs. Theoretically, at all events, they might be expected to prove of service, for once the control of the heat-regulating mechanism has been restored, any remedies which *facilitate the maintenance of this power*—such as any drugs which will diminish metabolism—ought to be of value. But so far as regards the treatment of hyperpyrexia in rheumatism when actually present, Wilson Fox's words, written in 1871, are equally applicable to the present day: "The fact remains, therefore, that at present the only agent on which reliance can be placed is the external application of cold" (14).[2]

Before passing on to consider the question of the prophylaxis of the condition, I would draw attention to a somewhat interest-

[1] *Brit. Med. Journ.*, 1893, ii. p. 993. [2] p. 32.

ing contribution to the treatment of hyperpyrexia in rheumatism by a French physician, H. Barré.

The frequent recurrence of this phenomenon, after it has once been checked by means of cold applications has already been referred to, one of the causes of death being not unfrequently cardiac failure from exhaustion following repeated excessive temperatures. It was in such a case as this, when the temperature, in spite of sodium salicylate and repeated baths, still tended to reach excessive limits, that Barré adopted the method of treatment by what he calls "disintoxication of the blood." The following is a summary of the notes of the case as recorded in the *Medical Press and Circular* (2)[1]:—

Girl, aged twenty, showing symptoms of acute rheumatism lasting eight days, during which the pains diminished under salicylate of sodium, and the temperature varied from 98·9° to 100°.

June 9 (the following day).—Restless; wandering; headache; pains ceased; temperature 104°. Bath ordered every three hours; 5 grammes of sod. salicylate given during the day. She felt better after the baths, but not for long. The temperature having risen to 105·4°, she was bathed every two hours. At 7 P.M. it was impossible to take her temperature. She had clonic and then tonic convulsions, which were succeeded by coma; her temperature at 11 P.M. being 107·6°. At 1 A.M. Barré applied his process, 500 grammes of blood being withdrawn from one arm, while the same amount of artificial serum was simultaneously injected into the corresponding vein of the opposite arm. The temperature then fell to 104·9°. The process was still further continued till 750 grammes had been exchanged, when consciousness returned, and her temperature was 103·2°. During the following day she slept calmly at intervals, the axillary temperature was 100°, and the baths were resumed along with the sodium salicylate. Improvement and ultimate recovery followed.

[I have throughout the above record converted the *Centigrade* temperature records into *Fahrenheit* for convenience in comparison with others cited.]

It is of course unjustifiable to draw conclusions from a single record, but, as previously mentioned, such a method of treatment suggests the possibility of some toxic product in the blood being the cause of the condition. At any rate the successful issue in Barré's case shows the propriety of trying the method in obstinate cases of hyperpyrexia in rheumatism. Fox has recorded in his book (14)[2] a case in which venesection to the amount of 20-30 ounces was practised with a view to combating the hyperpyrexia, but without effect, although the violent delirium ceased,

[1] p. 230. [2] p. 44.

and in which subsequent cold bathing failed to save the patient, though the temperature was reduced on each immersion. As his case, however, was complicated by the presence of "intensely fetid colliquiative diarrhœa," it can hardly be compared with Barré's, and at any rate the coincident transfusion of the artificial serum while venesection is being performed may enable the patient to withstand more easily the additional treatment by cold applications.

Prophylactic Treatment.

We now come to the second aspect of the treatment of hyperpyrexia—its prophylaxis. From the excessive mortality amongst the cases of acute rheumatism which develop this complication, it is evident that the question of its prevention is all-important, and still more so in view of the facts we have already seen, viz., that the earlier proper treatment is commenced before excessive temperature limits have been reached, the more hopeful is the prognosis. Are there, then, any means by which the occurrence of the dangerous complication described as rheumatic hyperpyrexia can be altogether prevented? To such a categorical question the reply, I think, can only be a decided negative. We have as yet no therapeutic measure by which the condition can be prevented, though we certainly do possess in cold applications a means whereby one of its manifestations—excessive temperature—can be prevented. But prophylaxis is made still more difficult in the case of this complication by reason of the fact that in many of the instances there is no warning of the condition whatever, and, as not infrequently is the case, the hyperpyrexia is *already present* without the patient or his friends being cognisant of the fact until (it may be a fortuitous) investigation of the body temperature reveals the fact, as in the case of the first example of the condition given in this paper. But for the fact that his medical attendant chanced to pay his daily visit at that hour the patient would not have learned that he was in a condition so dangerous that half an hour later he became comatose.

Fortunately, however, there are in many instances prodromal symptoms of sufficiently pronounced a character to attract the attention not only of his medical attendant but even his friends, and it is in such cases that there is an opportunity for the application of prophylactic treatment. The subject, however, presents points of difficulty. The most frequent precursor of hyperpyrexia in rheumatism is, as we have seen, *Delirium*. The Clinical Society's Report (7) [1] shows that out of 53 cases in which the date of occurrence of delirium with

[1] p. 270.

reference to the hyperpyrexia was noted, in no less than 24, or 45%, did it *precede*, and in 19, or 36%, *accompany* the onset of that condition. Now the fact of such a considerable percentage exhibiting this easily recognisable prodromal symptom would appear to suggest the likelihood of prophylactic treatment being frequently applicable.

But our *chief*—indeed one might say our *only*—preventive measure is the external application of cold to the patient, and the question that consequently arises is this—Does the *presence of delirium* in a case of acute rheumatism—not due, so far as can be made out by careful examination of the patient, to the presence of *visceral complications* such as *e.g.* pericarditis—warrant us in commencing treatment of the patient *by cold* applications even in cases in which the temperature is of quite a *moderately pyrexial* character or even *absolutely normal*? To show that cases do occur under this latter category, I need only refer to an instance in the Royal Infirmary, Edinburgh, of a patient under the care of Professor Fraser, by whose kind permission I am enabled to quote from his hospital records the following brief summary of those points which alone concern us here :—

Professor Fraser's case.—A school girl, G. O., aged twelve, was admitted to the Royal Infirmary on Oct. 21st, 1896, for acute rheumatism. "Characteristic rheumatic sour-smelling sweat; knees, ankles, and wrists are painful, but only the ankles are swollen." Under treatment by salicylate of soda the temperature was normal by the 23rd October.

24*th Oct.*—"Perspiring; nothing cardiac." *Temperature normal.*

25*th Oct.*—*Temperature normal.* Patient rather stupid in the evening and "wandering."

26*th Oct.*—*Temperature normal still.* Delirious; "occasional twitching of right hand." By evening she was "wildly delirious and shouting incoherently." No albumen in urine. *Temperature still normal.* Pulse 110.

27*th Oct.*—"Delirium now almost gone" (5.30 A.M.). Patient sinking into a state of coma. "*Temperature has now risen to* 100°." At 8.30 A.M. she was comatose, and at 10.30 A.M., when she died, the temperature had risen to 104·4°, an ice-cap having been applied to the head when the temperature reached 103°.

The autopsy revealed nothing to account for the condition, and a careful analysis made by Professor Fraser of the salicylate in use in the wards at the time, revealed no deleterious products in the drug.

Now, while it might be urged against my quoting this very interesting case that as a matter of fact up till the time of death the temperature had not reached the limit we have decided to

regard in this paper as hyperpyretic, there can be no doubt that the record is one of an instance of the same condition, although the patient succumbed before the temperature had risen to an extreme height. The important point, however, that we have to deal with at present is this.—Here was a patient in whom the onset of coma with rise of temperature was *preceded for nearly two days* by *delirium*, during which time *the temperature remained perfectly normal* (as shown by the four-hourly charts in the ward journals). There being, as stated in the record of the case, no cardiac or renal condition to account for this delirium, would *the treatment* of the condition *by cold* applications have been *justifiable*?

(*a*) Now, that the *application of cold* to *delirious hyperpyretic* patients is almost always followed by *subsidence* of the delirium and the *return of consciousness* is not only true but it is one of the most prominent and satisfactory characteristics of this method of treatment as already mentioned. (*b*) Another fact which we have also emphasised has, however, to be taken in conjunction with this—that *such application* of cold is followed by a *fall of temperature for some time after* the patient is removed from the cold bath or pack ; (*c*) while *reduction of his temperature* to *an excessive degree* as a result of this treatment is apt to be attended by dangerous, if not fatal, *collapse* of the patient. The difficulty in answering the question propounded above is now obvious. To apply for the *cure of the delirium* that remedy which is most likely to be successful is to subject the unfortunate patient to the *risk of collapse* as a consequence of such treatment ; while to *delay doing so* entails the risk attendant on those cases characterised by onset of delirium for some considerable time prior to the occurrence of the hyperpyrexia, in which, as we have previously seen,[1] the mortality is brought out by the Clinical Society's Report as very high. Were it possible to subdue the delirium by an application of cold so moderate as not to cause subsequent collapse of the patient, then, undoubtedly, such treatment is to be advocated ; but no one would, I think, be prepared to recommend the use of stronger measures, even though the probability of subsequent hyperpyrexia is quite recognised.

At what temperature treatment by means of cold should *be begun* is a question which is somewhat difficult to settle. The fact that delirium (of serious prognostic significance) may appear when the temperature is perfectly *normal* warrants one, I think, in saying that the time for adopting this treatment is to be decided rather by the *general condition* of the patient than merely the *state of his temperature*. Different writers vary as to the *height* to which the temperature should be allowed to rise

[1] p. 19.

before employing the cold bath. Thus *Fagge* says (13)[1]: "When the temperature is rising for the first time to a dangerous height it should not be allowed to reach 106° . . . before the bath is used. . . . Subsequently the bath should be had recourse to as often as the temperature rises to 105·5°."

Bryant, again, says (3)[2]: "When the temperature approaches 105° and particularly if nervous symptoms be present, a cold bath should be at once given"; while the *Clinical Society's Committee's* report of earlier date similarly indicates (7) "the advisability of having recourse to the bath where the temperature reaches 105°."

I cannot see any special reason for delaying so long before commencing the treatment by cold. The fact that cases not infrequently occur which prove *fatal before such a temperature* as 105° is *ever attained*, *e.g.*, the case of Professor Fraser's cited above, as also that group, in the Clinical Society's Report previously referred to, of "cases with the symptoms well-marked, characterising usually the hyperpyrexial cases *but without marked excess in temperature*," justifies one, I think, in advocating the earlier adoption of what is so well recognised as the most efficient remedy. It is rather interesting and significant to note that the statements in regard to the degree of temperature at which bathing should be employed are different in the *earlier* edition of Fagge's work (1884) where he says (13):[3] "When the temperature is rising for the first time it *should be allowed* to *reach 107°* . . . before the bath is used. . . . Subsequently it should be had recourse to as often as the temperature rises *to* 106°, but *not below* 105·5°." The tendency thus nowadays to commence vigorous treatment earlier than was formerly the custom is evident when these remarks are compared with the same authority as quoted above.

Briefly then, I would venture to suggest the following as a summary of the chief points in reference to the *prophylaxis* of rheumatic hyperpyrexia:—

1. Cases in which the pyrexia shows a tendency to *rise* instead of *decline* under full doses of the salicyl compounds, and in which *no intercurrent condition* can be detected which might account for the increasing pyrexia, *should be treated at once by cold applications without waiting for the onset* of *nervous symptoms or other prodromata of rheumatic hyperpyrexia.*

2. *When delirium appears in* a case which *exhibits pyrexia*, and no intercurrent visceral complication can be made out which might account for its presence, *the immediate employment of cold is called for.*

3. *Should delirium appear while the temperature remains normal* a *mild form of cold application—e.g. an ice-cap* to the head

[1] p. 712. [2] p. 400. [3] p. 548.

—should be employed, and on the appearance of *pyrexia* more *vigorous methods* ought to be adopted *without waiting for any extreme degree of pyrexia* (*e.g.* 105°) *to be reached.*

4. Cases *in which the hyperpyrexia* is, as it were, accidentally *discovered to be present* offer, of course, no field whatever for prophylaxis, but *treatment by cold should be commenced at once without waiting for the appearance of nervous symptoms or attempting to reduce the temperature by means of any antipyretic drugs.*

The preceding are merely put forward as a suggestion, but that there is a distinct need for more definite and decided teaching in our text-books on this subject of the treatment of rheumatic hyperpyrexia is shown, I venture to think, by records of cases, such as the following, in which treatment by medicinal remedies alone is relied on to combat the condition. It appeared [1] in a recent number of the *British Medical Journal* and, briefly summarised, is as follows :—

S. F., first seen *Jan.* 13*th*, suffering from rheumatic fever, "the heart labouring badly and a mitral murmur." Sod. salicylate gr. x four-hourly and a precordial blister were ordered.

Jan. 17*th*.—"The affected joints quite relieved, but from that time the daily temperature was about 105°." The salicylate was stopped in case it might be disagreeing.

Jan. 19*th* (midday).—The temperature was "fully 106°," and "she complained of a sinking feeling at her heart; slight tympanitic distension of the belly was noted, but otherwise she did not look very ill." Phenacetin in 10 grain doses was ordered, but of these she got only one. During the *night* the medical attendant was called and found her dying, the temperature in the axilla, "though this was wet with perspiration," being then 110·7°. "After the breathing had ceased for a short time" the heart was audible to the stethoscope, "beating regularly and distinctly."

It would seem that too often the somewhat vague teaching in most of our text-books as to the adoption of treatment by cold in this condition, leads to *delay* in the application until the *various phenomena* are *so fully developed* that the case then appears *too hopeless* to warrant such heroic treatment. Greater benefit might, I think, result from a clearer pronouncement on the use of this method, *to prevent* the occurrence of such a deadly complication.

There appears to be one other matter in regard to prophylaxis to which reference should be made.—Is it possible by a more efficient treatment of the *attack of rheumatism* in its *early* stages to prevent the occurrence of hyperpyrexia, or at anyrate diminish the tendency to it? On the hypothesis that hyper-

[1] *Brit. Med. Journ.*, 1898, vol. i. p. 618.

pyrexia is a result of exhaustion of the heat-regulating mechanism in its attempt to control the excessive heat-formations present in acute rheumatism, it would seem *theoretically* true, at all events, that the earlier this excessive heat-formation is put an end to, the sooner will the thermotaxic function return to normal, and hence paresis from exhaustion would be less apt to occur. Now if, as Maclagan suggests, the salicyl compounds act by destroying the rheumatic poison (which produces the excessive heat by its action upon the nidus present in the body), then obviously the earlier the patient is brought completely under the influence of the salicyl treatment the sooner will the excessive heat-formation be put an end to, and the strain taken off the thermotaxic mechanism. If this reasoning be correct, then, *another element* in the *prophylaxis* of hyperpyrexia will be the *early and complete subjection* of the case to the *salicyl compounds*. This, according to Maclagan, is to be obtained by the administration of hourly doses of 15-20 grains of salicine or sodium salicylate, by which a fall of temperature to normal should be obtained in forty-eight hours.

Finally, as pointed out by Fagge, every precaution should be taken to avoid all treatment, general or local, which would in any way tend to check perspiration. The skin plays such an important part in rheumatism as regards the elimination of heat through evaporation of sweat, that we should be very careful to prevent its free action being hampered in any way, directly or indirectly.

Whether the use of pilocarpin in those cases in which sweating has ceased prior to the onset of hyperpyrexia is likely to be attended with success, is a question on which I have not found any satisfactory evidence, although cases recording its use in this respect have been published. If the cessation of sweating arises, however, from *paresis* of the controlling mechanism, such a remedy would possibly be of little service.

Summary of Conclusions.

The main conclusions I would draw from the consideration of the whole subject of hyperpyrexia in rheumatism are these :—

1. That the condition is more prone to occur in the warmer months of the year, and apparently with greater frequency in certain years.

2. That while it is very difficult to estimate at all accurately the frequency of its occurrence, probably this is about ·5 per cent. amongst *adult* cases of rheumatism.

3. That the occurrence of hyperpyrexia in rheumatism is

practically confined to cases of this disease in persons over fourteen years of age.

4. That the rare instances of hyperpyrexia which occur under that age are in cases of rheumatism which present the *adult* type of the disease.

5. That the absence of hyperpyrexia from rheumatism in children is probably to be explained as the result of the *type* rheumatism assumes in them rather than a mere question of the *age* of the sufferer.

6. That *males* show a much greater proclivity to the condition than females, which may possibly be associated with the greater strain habitually put upon their thermotaxic mechanism.

7. That the condition is most apt to occur in "first attacks" of rheumatism.

8. That persons who have once suffered from the condition would probably be apt to have a recurrence of it in any subsequent attack of the disease (although no case of such recurrence has previously been published).

9. That it may ensue at any stage in an attack of rheumatism, but probably the second week is the most common period of its occurrence.

10. That it may arise in even *mild* cases of rheumatism, severe rheumatic symptoms being no essential to its occurrence.

11. That the onset of hyperpyrexia, while occasionally without warning, has usually premonitory symptoms, the chief of which is delirium.

12. That cases of true rheumatism showing *persistence of the pyrexia*, in spite of full doses of the salicyl compounds, should be most carefully watched, since hyperpyrexia frequently ensues in such instances.

13. That sudden cessation of the articular pains *without coincident fall of temperature* should lead to the suspicion of hyperpyrexia, especially if attended also by the cessation of sweating.

14. That Maclagan's hypothesis that hyperpyrexia is due to paresis of the heat-inhibiting mechanism from exhaustion in its attempt to control the excessive heat production of rheumatism, is the most feasible theory yet put forward in explanation of the condition, satisfactorily accounting for the more frequent occurrence of hyperpyrexia in adults than in children.

15. That the absence of rheumatic hyperpyrexia in children is a strong argument against the view that this condition is due to *visceral complications*, since it is especially in children that these visceral manifestations occur, and it is just in those cases that hyperpyrexia is not found.

16. That in view of the resemblance in several respects between rheumatic hyperpyrexia and "diabetic coma," further investigation of this subject might possibly throw fresh light upon the pathogenesis of both conditions.

17. That while the mortality of *rheumatism* is only about 3 per cent., hyperpyrexia is probably one of the most important immediate causes of death in this disease.

18. That the mortality of hyperpyretic cases is very high—probably over 50 per cent., but statistics are very variable because—

19. The mortality is greater the higher the temperature before treatment is begun; and

20. It is also greater amongst cases treated by means of antipyretic drugs alone.

21. That treatment by the application of cold in one of its various forms is the only justifiable method in cases of hyperpyrexia in rheumatism.

22. That this should be adopted even in cases apparently moribund, and even although visceral complications may be present.

23. That while there may possibly be some risk of congestion of internal organs as a result of this method of treatment, this does not justify the neglect of what is practically the only remedy for an otherwise fatal condition.

24. That the greatest care should be taken to prevent collapse ensuing in the patient as a result of the treatment by cold, which should be stopped entirely before the temperature falls to normal.

25. That antipyretic drugs, while practically useless in the treatment of hyperpyrexia *when present*, may perhaps be of some service in *preventing a recurrence* of this after the temperature has once been reduced by means of cold.

26. That in obstinate cases of recurrent hyperpyrexia the method of treatment by "disintoxication of the blood" adopted by Barré may probably be of service as an adjuvant to the treatment by means of cold.

27. That a greater attention should be paid to the *prophylaxis* of rheumatic hyperpyrexia, and that more prominence should be given to the advantage of commencing treatment by cold at an early stage before excessive temperatures are attained; in other words, the *general condition* of the patient, *rather than the mere height of his temperature*, should be the determining factor for commencing the treatment by cold.

28. That early and complete subjection of the patient to antirheumatic treatment would probably have some influence in preventing the occurrence of hyperpyrexia.

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